BRAIN.

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Original Articles and Clinical Cases.

SOME OBSERVATIONS ON THE GROWTH AND SURVIVAL-PERIOD OF INTRACRANIAL TUMOURS, BASED ON THE RECORDS OF 500 CASES, WITH SPECIAL REFERENCE TO THE PATHOLOGY OF THE GLIOMATA.[1]

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THE following observations form part of a general inquiry into the history, progress, treatment, fate, and, in many cases, the *post-mortem* findings of persons suffering from intracranial new growths who have come under observation at the National Hospital during the period of ten years, 1902-1911 inclusive.

I have here to make grateful acknowledgment of the permission of my colleagues to use the notes of their cases, and the ready help given me on all occasions, especially in the difficult matter of tracing the after-history of patients. As the numbers are large, and the notes in most cases voluminous, many being models of medical note-taking, it may not be out of place to say a word upon the method employed, especially as the value of some of the tables submitted depends entirely upon the accuracy of interpretation of the recorded clinical details, and the information received from the patients themselves, both of which constitute the main difficulty in an inquiry of this nature.

A careful abstract of the clinical features has been made upon a card under an index number, a running card-index of clinical points being made at the same time. This card also receives all other information that can be obtained, namely: (1) An account of operation, and further course of the case; (2) an abstract of the *post-mortem* examination—no small part of the task, which has been undertaken by my colleague

[1] Presidential Address (Section of Neurology), Royal Society of Medicine.

Dr. Howell, then pathologist, to whom I offer my best thanks; (3) an examination of the microscopical appearances; (4) all patients who have left the hospital have been written to—a circular letter with a short series of easily answered but sufficiently searching questions on the fly-sheet, and on the whole the answers have been intelligent, and of use in forming an opinion of the present state; 346 of these letters have been sent out, and 177 answers returned from patients or their friends; the remainder have not been answered, or the letters have been returned through the post. In forming tables of results, therefore, it has been necessary to assign a column of "No reply."

My junior colleagues, who have in the last ten years served on the Resident Staff, have kept in touch with some of these "No reply" cases to fairly recent dates, so this group affords some information of value. These facts are entered upon the cards.

During the ten years there have been in hospital 566 cases diagnosed as new growths, or as gummata. The gummata, 40 in all, have been rejected as requiring separate consideration. On close consideration, also, 26 cases have been eliminated for various reasons, not the least being the absence of optic neuritis. These rejections leave 500 cases of practically certain intracranial tumour, and it is from these that the facts and conclusions which follow have been gathered.

Table I presents the distribution of these tumours according to the regions of the brain involved. The larger number have been verified by operation or *post-mortem* examination. Many, of course, have been subjected to neither of these tests, but from the clinical details one may have little hesitation in accepting the diagnosis as correct, and these have been used for the estimation of the period of growth of tumours, whether still alive or since dead, without verification *post-mortem*.

To show how difficult is this question of rejecting or retaining cases in the absence of verification, I must refer to two cases amongst the rejections. The first, a woman, aged 43 (Dr. Beevor), who had suffered nineteen years before from severe fits, ten years torticollis, and frequent faints, five months posterior headache, five weeks a Jacksonian convulsion, left hand and arm preceded by an aura in the same situation. On admission she presented the picture of right precentral tumour: mental levity, intense optic neuritis, blurred vision, left hemiplegia, exaggerated left deep reflexes. The brain was explored by Sir V. Horsley over the region indicated, and nothing was found. There was much bulging afterwards, but the neuritis subsided to pallor, and she

became almost blind. Six weeks after operation she had a series of fits, beginning with purposive movements of the right arm, becoming clonic later, and, as the fit subsided, similar movements on the left side,

TABLE I.—REGIONAL CLASSIFICATION OF CASES OF ALL TUMOURS, WHETHER VERIFIED OR NOT.

Region	Sex		Total	Per cent.	
	M.	F.			
(1) Frontal	60	40	100	21·7	Fore-brain: 239. 52 per cent.
(2) Central pre- and post. Parietal	43	20	63	13·7	
(3) Temporo-sphenoidal ...	24	25	49	10·6	
(4) Occipital	8	6	14	3·0	
(5) Corona radiata; corpus callosum, &c.	4	6	10	2·1	
(6) Lateral ventricle	2	1	3	0·6	
(7) Pituitary	10	4	14	3·0	
(8) Optic thalamus	4	2	6	1·3	
(9) Mesencephalon	18	8	26	5·2	Mid-brain: 30. 6·5 per cent.
(10) Pineal	4	—	4	0·8	
(11) Choroid plexus; III and IV ventricles	4	1	5	1·0	
(12) Cerebellum	44	33	77	16·7	Cerebellum and pons: 160. 34·2 per cent.
(13) Extra-cerebellar	19	21	40	8·7	
(14) Pons	19	24	43	9·3	
(15) Medulla	—	1	1	0·2	
(16) Base	1	3	4	0·8	
Total	264	195	459		
(17) Not localized	24	17	41		
Grand total	288	212	500		

followed by coma. Nearly five months after she became alternately stuporose and noisy, again a series of right-sided fits, coma, and death from respiratory failure. *Post-mortem* no tumour was found, but great general rise of intracranial pressure, so as to force the posterior part of

the cerebellar lobes down into the foramen magnum—so-called pressure-cone. Dr. E. F. Buzzard made some 500 sections of the brain, and failed to find any cause for the symptoms. This may not be a rare case—in fact, there have been three similar cases—but if the *post-mortem* findings were not to hand it would have come into my table as a tumour of the Rolandic area.

The second case was of optic neuritis with swelling without localizing symptoms. This was rejected as a case of family optic neuritis. Her sister had been in hospital one year before with the same symptoms, and eventually quite recovered. Both had suffered from severe headache, parietal and frontal, and both had been diagnosed as tumor cerebri. Again, there may be many such.

Therefore the group " Not localized " has little value, and is placed by itself in this table. It has been used in Table II, age-incidence, but in the other tables in which it occurs it is taken by itself on its own merits.

There can be little doubt that a fair number in this group are Frontal and Temporo-sphenoidal cases, latent or of slow growth; some may be deeply seated subcortical growths in the Corona radiata or ventricles, regions of indefinite symptomatology. It will be seen that the two most vulnerable regions are the Frontal and the Cerebellum. But if we take the Frontal and Parietal together, which, considering the great tendency to overlapping, is a reasonable thing to do, and for the same reason we link together the Cerebellum and Pons, it is remarkable how closely in the respect of vulnerability these two antipodal regions correspond—i.e., Fronto-parietal 163 cases, Ponto-cerebellar 160—making together more than half the total of all growths, whether verified or not, for all regions.

In the Fore-brain, which includes the first six regions in Table I, and which claims 52 per cent. of the whole number, the Frontal group heads the list with 100 cases, 21·7 per cent. of the total, and 41·8 per cent. of the Fore-brain. We have much exact knowledge both of localization, and of the characters, of the growths of this region, by reason of the fact that operations have been performed in 74 per cent. of the cases. The Central group is smaller, 63, but owing to the comparatively clear and definite symptomatology of the motor region, operations have been performed in a yet larger percentage of cases—i.e., 52 out of 63, or 82·5 per cent.

Of tumours of the Temporo-sphenoidal region we have a fair number, 49. The diagnosis of lesions of this region is among the most difficult,

TABLE II.—AGE AT APPEARANCE OF FIRST SYMPTOM FOR ALL GROWTHS, VERIFIED OR NOT.

Region	Sex		Total	1—20 years		21—30 years		31—40 years		41—50 years		51—60 years		61—70 years	
	M.	F.		No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
(1) Frontal	60	40	100	9	9·0	30	30·0	39	39·0	14	14·0	7	7·0	1	1·0
(2) Central (parietal)	43	20	63	9	14·2	12	19·0	19	30·0	16	25·3	6	9·5	1	1·5
(3) Temporo-sphenoidal	24	25	49	10	20·4	14	28·5	18	36·7	5	10·2	2	4·0	—	—
(4) Occipital	8	6	14	2	14·2	4	28·5	1	7·1	3	21·4	4	28·5	—	—
(5) Corona radiata, corpus callos., &c.	4	6	10	1	10·0	3	30·0	—	—	2	20·0	4	40·0	—	—
(6) Lateral ventricle	2	1	3	1	33·3	—	—	2	66·6	—	—	—	—	—	—
(7) Pituitary	10	4	14	2	14·2	6	42·8	4	28·5	2	14·2	—	—	—	—
(8) Optic thalamus	4	2	6	1	16·6	1	16·6	2	33·3	2	33·3	—	—	—	—
(9) Mesencephalon	18	8	26	12	46·1	9	34·6	3	11·5	1	3·8	1	3·8	—	—
(10) Pineal	4	—	4	1	25·0	2	50·0	—	—	1	25·0	—	—	—	—
(11) Choroid plexus, III and IV ventricles	4	1	5	1	20·0	2	40·0	—	—	2	40·0	—	—	—	—
(12) Cerebellum	44	33	77	47	61·0	14	18·1	10	14·2	3	3·8	3	3·8	—	—
(13) Extra-cerebellar	19	21	40	5	12·5	7	17·5	19	47·5	6	15·0	2	5·0	1	2·5
(14) Pons	19	24	43	23	53·4	7	16·2	8	18·3	5	11·6	—	—	—	—
(15) Medulla	—	1	1	1	—	—	—	—	—	—	—	—	—	—	—
(16) Base	1	3	4	1	25·0	—	—	—	—	1	25·0	2	50·0	—	—
(17) Not localized	24	17	41	13	31·7	12	29·2	12	29·2	2	4·8	2	4·8	—	—
Totals	288	212	500	139	—	123	—	137	—	65	—	33	—	3	—

yet a large number, 32, or 65·1 per cent., have come to operation and with a lower mortality than in the two preceding groups. The occipital group is much smaller, only 14, and as the localization is not difficult owing to the rather sharp symptomatology referable to the optic radiations and angular gyrus, it may be inferred that tumours in this region are comparatively rare. Operations have been performed in seven cases—i.e., 87·7 per cent. The Mid-brain group includes 26 cases, to which may be added the Pineal cases, making together 30, or 6·5 per cent. of the whole. The diagnosis of these lesions has been made more practicable by the work of Head and Holmes, and probably in the future the percentage of this group will be higher, but I fear surgery offers little hope of help in dealing with such cases.

The Cerebellum proper offers 77 cases, 16·7 of the whole, and as the clinical indications are fairly well marked, this is probably a true figure; 36, or 46·7 per cent., have been verified by operation.

Of the Extra-cerebellar group, 5 are Gliomata and 13 Fibrogliomata, and therefore primary in the Cerebellum, but as their line of growth was almost entirely in the lateral recess, I have included them in this group. There were 40 in all, and 32, or 80 per cent., came to operation.

Of tumours of the Pons there were 43, or 9·3 per cent.; they require no comment in this connexion.

Growths of the Medulla must be very rare. I find record of only 1, an infiltrating Glioma.

Table II: Age at appearance of first symptom.—This, of course, is not necessarily a true indication of the age of the tumour, which may have existed in a latent state for any length of time. The table requires little comment. Its value is regional only. Of tumours of the Fore-brain generally, 142, or 59·4 per cent., made their first manifestation between the ages of 21-40; 32 only, or 13·4 per cent., between 1-20; 63, or 26·7 per cent., between 41-60; and only two in the last decennium, one of which was strictly 72.

Of the Mid-brain group 21, or 80·7 per cent., appeared first between ages 1-30, 12 of these falling between 1-20. Of the Ponto-cerebellar tumours (excluding Extra-cerebellar; in 70 cases, or 58·3 per cent., symptoms appeared first between 1-20, 21, or 17·3 per cent., between 21-30, 18, or 15 per cent., between 31-40, and only 8, or 6·6 per cent., between ages 41-50.

But the Extra-cerebellar group more nearly resembles in age-incidence the Fore-brain tumours, in that the larger number, 19, or 47·5 per cent., fall between ages 31-40.

TABLE III.—AGE AT APPEARANCE OF FIRST SYMPTOMS FOR GROWTHS OF WHICH THE NATURE HAS BEEN VERIFIED ON OPERATION OR POST-MORTEM.

Nature of growth	1—20 YEARS				21—30 YEARS				31—40 YEARS				41—50 YEARS				51—60 YEARS				61—70 YEARS				Total	Per cent.
	M.	F.	Total	Per cent.	M.	F.	Total	Per cent.	M	F.	Total	Per cent.	M.	F.	Total	Per cent.	M.	F.	Total	Per cent.	M.	F.	Total	Per cent.		
Glioma ...	9	16	25	19·6	25	12	37	29·1	25	7	32	25·1	14	5	19	14·9	8	5	13	10·2	—	1	1	0·7	127	49·2
Fibroglioma ...	—	2	2	13·3	—	4	4	26·6	2	4	6	40·0	1	2	3	20·0	—	—	—	—	—	—	—	—	15	5·8
Fibroma ...	2	2	4	30·7	—	—	—	—	7	2	9	69·2	—	—	—	—	—	—	—	—	—	—	—	—	13	5·0
Endothelioma	4	2	6	16·2	2	2	4	10·8	8	8	16	43·2	7	2	9	24·3	1	1	2	5·3	—	—	—	—	37	14·3
Sarcoma ...	3	—	3	14·2	5	—	5	23·8	5	1	6	28·5	3	3	6	28·5	—	1	1	4·7	—	—	—	—	21	8·1
Carcinoma ...	—	—	—	—	—	—	—	—	3	—	3	20·0	3	3	6	40·0	3	2	5	33·3	1	—	1	6·6	15	5·8
Tuberculoma	4	5	9	64·2	2	2	4	28·5	1	—	1	7·1	—	—	—	—	—	—	—	—	—	—	—	—	14	5·4
Cyst, simple ...	3	—	3	60·0	2	—	2	40·0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5	1·9
Papilloma ...	—	—	—	—	1	—	1	33·3	—	—	—	—	1	1	2	66·6	—	—	—	—	—	—	—	—	3	1·1
Cholesteatoma	—	—	—	—	—	1	1	—	1	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	2	0·7
Pituitary ...	—	—	—	—	1	—	1	—	1	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	2	0·7
Pineal ...	1	—	1	—	2	—	2	—	—	—	—	—	1	—	1	—	—	—	—	—	—	—	—	—	4	1·5
Totals ...	26	27	53	20·5	40	21	61	23·6	53	22	75	29·0	30	16	46	17·8	12	9	21	8·1	1	1	2	0·7	258	—

To sum up briefly, it would appear that tumours of the Fore-brain tend to appear more frequently in middle age, but no age is exempt. Those of the Mid-brain, on the other hand, appear first predominantly in the early or adolescent period, and the same may be said of the Cerebellum and Pons; comparatively few occur after 30.

Table III has perhaps more interest than the last, and though the figures are smaller they include verified cases, and are therefore of more value. The Gliomata come first, 127, or 49·2 per cent., and it is seen that the numerical age-incidence for each decennium to 50 is fairly similar, but the largest number falls between 21-40. The Fibrogliomata are few, but they conform in this respect with the last.

The same may be said of the Endotheliomata: the largest number, 16, or 43·2 per cent., of the group falling between 31-40.

The Sarcomata show practically the same age-incidence.

Carcinomata, as might be expected, appear in later periods, 31-60, but they are few.

Tuberculomata also are few, 14 only; of these 9 appear between 1-20, and only 1 between 30-40. The remaining growths are too few to base any conclusions upon.

Heredity.—In the records of cases heredity receives due attention. The class of patients at this hospital, generally speaking, is perhaps somewhat above that of general hospitals, so that diseases so striking as tumour of the brain, or cancer, might be expected not to be overlooked by the patient or friends. Yet among the 500 cases I find a cancerous heredity in no more than 37 cases, or 7·2 per cent. Of these 13 were in the father and 2 others on his side, 15 in the mother and 2 others on her side, 1 brother, 3 sisters, 1 aunt. In 10 the growth in the patient was Glioma, in 2 Fibroglioma, in 4 Fibroma, in 2 Endothelioma, and in 1 Tuberculoma. In 17 the nature of the growth was not known.

In no case is there any family history of tumor cerebri. We may assume, then, that heredity is a negligible factor.

Table IV: Regional incidence of growths verified on operation or *post-mortem* examination.—The accuracy of this table depends upon the correct interpretation of the microscopical appearances of the section preserved, and some of them are so puzzling that their proper place in this table is almost a matter of opinion. With this reservation the table may be considered for practical purposes a true statement.

Glioma.—It is evident that of all growths the Glioma is the largest in number and the most universal in its incidence. Of the total 258

TABLE IV.—REGIONAL INCIDENCE OF GROWTHS VERIFIED ON OPERATION OR POST-MORTEM.

Region	No. of growths for each region	Glioma		Fibroglioma		Fibroma		Endothelioma		Sarcoma		Carcinoma		Tuberculoma		Cyst		Papilloma		Cholesteatoma		Pituitary		Pineal adenoma	
		No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent
(1) Frontal ...	68	38	55·8	—	—	—	—	21	30·8	4	5·8	4	5·8	1	1·4	—	—	—	—	—	—	—	—	—	—
(2) Central ...	43	25	58·1	—	—	—	—	10	23·2	3	6·9	5	11·6	—	—	—	—	—	—	—	—	—	—	—	—
(3) Temporo-sphenoidal	27	17	62·9	—	—	—	—	4	14·8	2	7·4	2	7·4	2	7·4	—	—	—	—	—	—	—	—	—	—
(4) Occipital ...	6	4	66·6	—	—	—	—	—	—	1	16·6	1	16·6	—	—	—	—	—	—	—	—	—	—	—	—
(5) Corona radiata, corp. callos.,&c.	8	6	75·0	—	—	—	—	—	—	1	26·5	1	26·5	—	—	—	—	—	—	—	—	—	—	—	—
(6) Lateral ventricle	3	1	33·3	—	—	—	—	—	—	2	66·6	—	—	—	—	—	—	—	—	—	—	—	—	—	—
(7) Pituitary ...	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
(8) Optic thalamus	3	1	33·3	—	—	—	—	—	—	2	66·6	—	—	—	—	—	—	—	—	—	—	2	—	—	—
(9) Mesencephalon	8	4	50·0	—	—	—	—	—	—	1	12·5	—	—	2	25·0	1	12·5	—	—	—	—	—	—	—	—
(10) Pineal ...	4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4	—
(11) Choroid plexus, III and IV ventricles	4	—	—	—	—	—	—	—	—	1	25·0	—	—	—	—	—	—	3	75·0	—	—	—	—	—	—
(12) Cerebellum ...	34	18	52·9	—	—	1	2·9	1	2·9	3	8·8	1	2·9	6	17·6	4	11·7	—	—	—	—	—	—	—	—
(13) Extra-cerebellar	32	5	16·3	13	40·6	11	34·3	1	3·1	—	—	—	—	—	—	—	—	—	—	2	6·2	—	—	—	—
(14) Pons	12	7	38·3	1	8·3	1	8·3	—	—	—	—	—	—	3	24·9	—	—	—	—	—	—	—	—	—	—
(15) Medulla ...	1	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
(16) Base crus, &c....	3	1	33·3	—	—	—	—	—	—	1	33·3	1	33·3	—	—	—	—	—	—	—	—	—	—	—	—
Totals ...	258	127	49·2	15	5·8	13	5·0	37	14·3	21	8·1	15	5·8	14	5·4	5	1·9	3	1·1	2	0·7	2	0·7	4	1·5

growths, 127, or 49·2 per cent., were Gliomata. Grouping the regions as before, we find there are 91 Gliomata, or 58·7 per cent. of all growths in the Fore-brain. Again, in the Mid-brain this class of tumour predominates to the extent of 50 per cent., but the numbers are few. In the Cerebellum and Pons, including the Extra-cerebellar growths, there are 30 Gliomata out of a total of 78, or 38·4 per cent.

Fibroglioma and fibroma.—These are peculiar to the Cerebellum and Pons and the one Medulla case. The Fibroglioma is a growth which presents the features of Glioma and Fibroma, and I cannot yet say whether it is a distinct pathological entity or a true Glioma in which the conditions of growth are in some way modified by its surroundings. I am inclined to think the latter, and if so it should be included among the Gliomata.

In the peripheral parts of some of the Gliomata in the Fore-brain a tendency to the formation of fibrous stroma with elongation of nuclei is frequently seen, even to the extent of rough capsulation.

Endothelioma.—Endotheliomata are much less common, and they occur practically only in the anterior fossæ of the skull. The regions involved are therefore the Frontal 21, Central 10, and Temporo-sphenoidal 4. Two only affected the posterior fossæ, one in the lateral recess and the other compressing the vermis. To these must be added two Cholesteatomata, which were Extra-cerebellar. This is a curious and interesting point, and it is difficult to explain why the endothelium of the falx, and only the anterior part of it, should be affected to the exclusion almost of all the rest of the great dura matral sheath. There were 35 Endotheliomas of the three regions named, or 25·3 per cent. of all growths for those regions.

Sarcoma.—This group presents some difficulty in classifying, for, as will appear later, there are stages in the growth of the Glioma which, if universal in the section, may be almost indistinguishable from some of the recognized forms of Sarcoma. In any case the group is not a large one. Twenty-one cases only, or 8·1 per cent. of the whole. Six were undoubted round or spindle-celled Sarcomas, 3 of them secondary growths, 1 to suprarenal, 1 to kidney, and the other, melanotic, to the eye. The remainder were primary, and no part of the brain can be said to be exempt.

Carcinoma.—Primary carcinoma is interesting from its comparative rarity. Of the total (15) 1 only is undoubtedly primary, and, from its peculiar appearance, of the Choroid plexus. Seven may have been primary, that is, no growth was found elsewhere, but in one or two only

the brain was allowed to be examined. The remaining 7 were secondary—the primary growth being mammary in 3, ovarian, suprarenal, pancreatic and rectal in the other 4.

Tuberculoma.—Verified cases are surprisingly few. It is often diagnosed, but deaths are few. The age-incidence is so young that no doubt large numbers of these patients go to children's and general hospitals. It is also probable that many recover, and I suspect that many of the long survival-periods may include this class of tumour.

Cyst.—The simple cyst deserves attention. I can find record of only 5 in which the true character was verified. All were thin-walled, apparently structureless bags containing clear fluid. One was found *post-mortem* in the mid-brain lying ventrally to the Sylvian aqueduct. The patient died unrelieved by a cerebellar decompression. The others were in the cerebellum, and three came to operation. Two of them were successfully drained and the patients were known to be alive and well six or seven years after ; in the other, by a mistake in localization the exploration was made on the wrong side and the patient died seven days after. The fifth case presented an uncertain symptom picture, though a Mid-cerebellar growth was suspected; no operation was attempted and the patient died fifteen months after the first symptom in the London Hospital. The Medical Registrar has kindly sent me an abstract of the autopsy, at which was found a very thin-walled cyst, of the size of a golf-ball, lying between the two lobes of the cerebellum and pressing down upon the floor of the fourth ventricle. Here is a case that must fill one with regret; operation might reasonably be expected to have been quite successful. If simple cysts were common, that in itself would almost justify exploration in any cerebellar case indiscriminately, but 5 in 258 is 1·9 per cent., and if this is anywhere near the truth simple cyst is a rare condition. Many gliomas, one may say most of the more chronic forms, develop cysts containing semi-gelatinous fluid, the drainage of which often affords more than temporary mechanical relief, but there is little evidence that the ultimate growth of the tumour is to any extent modified.

Papilloma.—Papilloma of the Choroid plexus is a rare condition; it occurred in 3 cases only. In one the growth was felt in the middle peduncle of the right lobe of the Cerebellum, and as much as possible was removed, but the patient died ten days after. Another patient died of pneumonia, and the third died outside, but Dr. Holmes made an autopsy and found a Choroid plexus tumour undergoing colloid degeneration. These growths present the appearance of simple adenomatous overgrowths

of the normal tissue, but clinically they are as dangerous to life as any malignant growth, and their situation is such as to be out of the range of successful operation, even if they could be diagnosed with certainty.

The only case of undoubted primary carcinoma, alluded to above, presented the general features of a Choroid plexus tumour, but the columnar cells of the papilloma are swollen into great round cells undergoing active multiplication. In this case also there were many small islands of secondary growth, mostly cortical, the largest being in the left Rolandic region. This region was explored and a cyst punctured, with the escape of 1 c.c. of colloidal fluid. The patient died of respiratory failure on the table. A papilloma, then, may take on highly malignant features.

Cholesteatoma.—One undoubtedly presented the characteristics of this class of tumour. It was Extra-cerebellar in situation, found on operation in the right lateral recess, and removed successfully, but unfortunately the patient died seventy-five days after of sepsis. The tumour was encapsuled, and on incision exuded white, glistening, pultaceous matter consisting largely of cholesterin, and also some large epithelial cells. It proved impossible to preserve the crystals and the section now shows a structureless network with some granular detritus in its meshes. The other was also Extra-cerebellar deeply in the right lateral recess. It was removed successfully piecemeal. The patient was seen a year after, but was in a very poor condition, with all the old symptoms, severe vertigo, and ataxia, with mental enfeeblement and a large hernia. The tumour was described as white, hard, and encapsuled, but no cholesterin was noted at the time of operation. The section now is strikingly like the last.

It is probable that these growths are highly degenerate endotheliomata, and it is perhaps an unnecessary refinement of classification to place them in a group apart.

Pituitary.—The clinical features of pituitary tumour referable to pressure on the Chiasma are so marked that the number 14, or 3 per cent. of the whole, probably represents the true percentage, though only 4 have been verified, all by operation. In 3 of these the tumour was removed more or less completely, and in the fourth partially only, the state of the patient becoming so bad that operation had to be suspended and the patient died nine hours after without recovering consciousness. Of the 3 that survived 2 died in about six months and the third survived three and a half years. It is probable that recurrence took place, and therefore a considerable degree of malignancy

must be ascribed to these growths, at any rate if disturbed by operation. This result should be compared with the long survival of pituitary tumours considered below.

Pineal.—Clinically these tumours are undiagnosable as such, the symptoms being referable to Mid-brain and internal hydrocephalus. There have been 4 cases in the ten years, 3 of which have been reported by Howell. The growth, which is of the nature of adenoma or adeno-sarcoma, tends to fill the third ventricle and to extend down the aqueduct of Sylvius to the fourth ventricle, infiltrating more or less widely the surrounding structure.

The Survival-period of Tumours from the Appearance of the First Symptom to Death.

I now come to a most interesting part of the subject, an inquiry into the life-history of such tumours as have been verified *post-mortem*, untouched by surgery, which therefore may be assumed to have run a natural course, for it is idle to suppose that, in the present state of knowledge, any therapeutic agent can modify, to any extent, the growth of any of the tumours now under consideration except the tuberculomata. And yet it must be within the experience of every physician that in many cases an extraordinary change for the better occurs during the period of rest and observation in the wards, so that important symptoms, pain, vomiting and the like, disappear, and even optic changes regress. This adds another difficulty in deciding upon the advisability of operative interference.

Table V includes patients who died in the wards and on whom a *post-mortem* examination was made. There were 65 of these, and the average in months of survival from the first symptoms is given for the regions and growths.

In the last column, "Not verified," is given the same average for patients in whom the diagnosis was reasonably certain, but who died outside, or on whom autopsy was not allowed; they number 43.

These periods are of sufficient significance to justify some consideration in detail, especially as the survival-period after operation is of paramount interest, which must be enhanced by comparison with these. The results of operations in this respect will form part of a report to the International Congress of Medicine in 1913.

Glioma.—If we take the 22 gliomata of the Fore-brain as a whole, we find that the patients survived for all sorts of periods from six

weeks to nine years, and if we strike a rigid average for all these periods it is found to amount to 16·2 months. But among these 22 is one most exceptional survival-period, nine years, so much so that it seems justifiable to exclude it, and strike an average of the remaining 21. The result of this is to bring the average survival-period down to 10·1 months, and I think this is probably not far from the truth. It may be in excess somewhat because there were three other rather exceptional periods, namely, of four, four and a half, and three years, but on the other hand more cases to deal with might show still more of these long periods.

It will be noticed that the survival-period in cases of tumour of the Frontal region is the longest; the Temporo-sphenoidal region comes next with fewer figures, and the Corona radiata last with still fewer. The Central and Occipital are too few to be considered separately.

The Mid-brain, Ponto-cerebellar and Base (interpeduncular space) may be fairly taken together, though the number of cases is small, 11 in all. The shortest survival-period was twenty-four days, a case of glioma of the Pons, and the longest was two years, also of the Pons. The average survival-period for the 11 cases was 9·4 months, not much less than that for the Fore-brain.

Fibroglioma and fibroma came to operation in all cases but the two on this table.

Endothelioma.—There are too few to base conclusions of any value, 4 in the Fore-brain and 2 in the Cerebellum. These 6 give an average survival of 20·2 months. A rough estimate of the period of growth may be arrived at by averaging the period from the first symptom to the time of operation, in the operation cases, disregarding the result, whether good or evil. Perhaps this may give truer results than at first appears likely, for in some of the cases a fatal issue in any case could not have been long deferred. Thirty-one cases are available for this purpose with very variable survival-periods, for instance, 1 of twenty years or more, another of eighteen years, 3 of ten years, and the rest of all periods from seven years to six months, 1 only of two months. A strict average for all these gives four years as the average survival-period for this class of tumour, and on the whole this may not be far from the truth, though probably it errs on the side of under-estimation.

Sarcoma.—The figures again are few, only 5. The survival-period averages 11·2 months. One patient, however, with a sarcoma of the Optic thalamus, survived four years, which must be an extreme time for

TABLE V.—AVERAGE SURVIVAL PERIOD IN MONTHS FROM FIRST SYMPTOM TO FATAL TERMINATION. NATURE OF GROWTH VERIFIED POST-MORTEM.

Region	Glioma		Fibroglioma		Fibroma		Endothelioma		Sarcoma		Carcinoma		Tuberculoma		Cyst		Papilloma		Not verified		Totals
	No.	Average in months	No.	Average in months	No.	Average in months	No.	Average in months	No.	Average in months	No.	Average in months	No.	Average in months	No.	Average in months	No.	Average in months	No.	Average in months	
(1) Frontal... ...	9	16	—	—	—	—	2	10 : 72	—	—	2	8	—	—	—	—	—	—	6	39	19
(2) Central... ...	2	7 : 108	—	—	—	—	1	4	1	2·5	1	7	—	—	—	—	—	—	3	6	8
(3) Temporo-sphenoidal	6	9	—	—	—	—	1	9	—	—	1	8	—	—	—	—	—	—	2	—	10
(4) Occipital ...	1	5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	19	2
(5) Corona radiata ...	4	7	—	—	—	—	—	—	1	5	1	5	—	—	—	—	—	—	1	5	7
(6) Lateral ventricle	—	—	—	—	—	—	—	—	1	1·7	—	—	—	—	—	—	—	—	—	—	1
(7) Pituitary ...	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	48	1
(8) Optic thalamus ...	—	—	—	—	—	—	—	—	2	6 : 48	—	—	—	—	—	—	—	—	1	30	3
(9) Mesencephalon ...	1	5	—	—	—	—	—	—	1	1·5	—	—	2	1·1 : 6	—	—	—	—	2	10 : 18	6
(10) Choroid plexus ...	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2	7 : 24	—	—	2
(11) Cerebellum ...	2	12	—	—	1	7	1	3	—	—	1	10	2	13 : 108	1	15	—	—	7	20	15
(12) Extra-cerebellar...	2	6 : 18	—	—	—	—	1	12	—	—	—	—	—	—	—	—	—	—	2	12 : 33	5
(13) Pons	5	9	1	10	—	—	—	—	—	—	—	—	3	7	—	—	—	—	11	21	20
(14) Base	1	2	—	—	—	—	—	—	1	12	1	24	—	—	—	—	—	—	1	22	4
(15) Not localized ...	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5	48	5
Totals ...	33	—	1	—	1	—	6	—	7	—	7	—	7	—	1	—	2	—	43	—	108

Where the number is more than two, averages are given. If only two, the survival-period for each is given, unless the two periods are almost equal. Decimal points omitted, except in single cases.

sarcoma. If we drop this, the remaining sarcomas give a period of 5·1 months, which perhaps is an under-statement.

Carcinoma.—Seven cases give an average survival-period of 10·1 months, probably an over-statement.

Tuberculoma.—In any case verified Tuberculomata are few, 14, 7 of which came to operation. The 7 that remain give a strict average survival-period of 21·5 months, but in one case the growth had been in existence nine years; without this the survival falls to seven months. However, taking the survival-period to the time of operation, as was done in dealing with the endotheliomata, we find an average survival-period of 17·4 months. The probable explanation of these varied results is that tuberculomas present in their development periods of activity and of quiescence, determined by varying degrees of constitutitional resistance, and it is not too much to assume that such periods of latency may ultimately become permanent. This must surely be the explanation of some of the results shown in Table VI. The importance of an early tuberculin test need scarcely be urged, in view of medical treatment, for the results of surgical interference are far from encouraging.

Simple cyst.—One might expect a simple cyst to be associated with a long survival-period. Only one is forthcoming as fatal without interference, and that had given symptoms for fifteen months (*vide supra*). Mechanical pressure on the floor of the fourth ventricle no doubt was the immediate cause of death. But one can form no conception of how long this cyst had been in existence before making itself felt, and this, of course, applies to all growths. Four came to operation, and in them the survival-period averaged 12·3 months. Apparently these cysts, though rare, are progressive in their enlargement, and their progress is fairly rapid.

Papilloma.—Two cases ran a natural course and, as shown in Table V, survived seven months and two years respectively. Two came to operation and had shown symptoms six months and twelve months to the time of operation. One of these patients was alive four and a half years after. No conclusion can be arrived at in so few instances.

The column "Not verified" includes 43 cases in which the localization was sufficiently clear to justify placing them in the regions named. For various reasons operation was not thought advisable, or in a fair number of cases was refused by the patient. All these patients left hospital alive, and having been written to, the information has come to hand that they have since died, and generally a date has

been given. Some died in hospital, but an autopsy was refused. Of course, we have no idea of what class these tumours were, but nevertheless the survival-period is worthy of note. Averaging the 43 cases, we arrive at a survival-period of 24·3 months, a little over two years. The largest number of these, 20, are of Cerebellum and Pons.

TABLE VI.—AVERAGE SURVIVAL PERIOD IN YEARS FROM FIRST SYMPTOM FOR PATIENTS ALIVE OR FROM WHOM NO INFORMATION HAS BEEN RECEIVED. NATURE OF GROWTH NOT KNOWN.

Region	Alive to date		No reply		Total
	Number	Average in years	Number	Average in years	
Frontal	2	2 : 6	5	1·3	7
Central	—	—	3	2·6	3
Temporo-sphenoidal	2	4·6 : 6	5	2·4	7
Occipital	2	18	3	5·2	5
Corona radiata	—	—	—	—	—
Lateral ventricle	—	—	—	—	—
Pituitary	7	9·7	2	2·5 : 0·5	9
Optic thalamus	1	9	1	3	2
Mesencephalon	6	6·5	7	3·4	13
Choroid plexus	—	—	—	—	—
Cerebellum	13	5·7	13	1·4	26
Extra-cerebellar	—	—	3	2·5	3
Pons	5	6·9	12	1·5	17
Base	—	—	—	—	—
Not localized	13	5·2	19	2·8	32
Totals	51		73		124

There remains for consideration Table VI, which seems to me to be of some interest in spite of many weak points. It concerns a total of 124 cases of more or less clinically certain tumours of the Brain, 22 in the Fore-brain, 9 Pituitary, 20 in the Mid-brain, 46 in the Cerebellum and Pons, and 32 not localized at all. These cases fall in an

"Alive to date" column, 51, and of these I have certain information as to their survival and some idea as to their present condition, and a "No reply" column, 73; letters to the patients have been returned through the post.

A glance at the first column suffices to show a remarkably long survival-period. The average, excluding the Pituitary group which deserves special notice, is 6·3 years. Grouping the regions as in former calculations, we find the Fore-brain gives the long survival-period to date of 9·5 years, but this is exaggerated by 2 Occipital cases of eighteen years, 1 probably a tuberculoma.

The Mid-brain and Optic thalamus together, 7 cases, give an average of 6·9 years, and the Cerebellum and Pons, 18 cases, in the same way give a survival-period of six years to date.

The Pituitary groups seem to possess special significance examined in this manner, because the symptomatology of these tumours is so distinctive. It includes 7 cases. All had more or less intense optic atrophy, with progressive loss of sight, and at some time characteristic hemianopsia, though one patient replies that his sight has improved. The average survival-period for all of these is 7·5 years to present date. All of them had been diagnosed as pituitary cases, 2 seem doubtful, but their removal does not appreciably affect the average. Even if this is a gross over-statement it would appear that the growth of these tumours is naturally a slow one, and this is significant in view of the tendency to recurrence after operative treatment (*vide supra*).

In the "No reply" column the survival-period is naturally less striking, because it has to be calculated to the date at which the patient left hospital. It is therefore of little value, but the average survival to that date is 28·4 months. Many of these, of course, may not be alive.

Now I give these figures for what they are worth and they must be received with great caution; but they are sufficiently large to arrest attention and provoke speculation, too large, I think, to be ignored. Probably a certain number are gummata without a history of syphilis, many no doubt are tuberculomata, but it is quite possible that among them are quiescent or latent gliomata or endotheliomata. This is pure speculation, but I would recall the not infrequent instances of a long survival-period among the verified cases, proving that glioma even, and endothelioma certainly, may run very long courses. It is also significant that the cerebellum should supply a proportionately large number of the cases, namely, 26, 13 of which are alive still with an average sur-

vival of five and a half years; an equal number from whom no reply has come give an average of 1·4 years to the time of leaving hospital, which perhaps might safely be doubled or even trebled, but equally, of course, some may not be alive. The symptomatology of cerebellar tumours is sufficiently distinctive so that the margin of error in diagnosis can scarcely be very great. The obvious objections to a table of this kind are the initial possibility of error in diagnosis, and ignorance of the nature of the lesion; so much has to be taken on trust, and the danger is that it may be taken too literally.

An Inquiry into the Life-history of the Glioma from the Histological Standpoint.

Of all the growths that affect the brain the glioma stands first both in frequency and importance.

As shown above, of 258 cases in which the nature of the growth was verified 127, or 49·2 per cent., were of this class. Most of these I have examined myself, thanks to the labours of our pathologists during the last ten years, and they present a bewildering variety of histological appearances, and the difficulty of placing some of them seems almost insurmountable. This difficulty is rendered all the greater from the fact that the same tumour may present, sometimes within the compass of an ordinary section, grades of change of great variety, so that at one end of the section we are looking at an apparently innocent growth, and at the other a richly cellular mass, more like a malignant sarcoma, or in another place an area of necrosis. On the whole, this variety of appearances seems to be distinctive of the gliomata, and occurs more often, and in a higher degree, among them than in any other of the intracranial growths. To arrive at a just estimate of the malignancy of a glioma it is really necessary to make sections from the periphery to the centre, and this of course, is not always possible.

The original conception of a glioma is that of a simple overgrowth of the connective tissue element of the brain. It is not common to find a tumour which presents this simple character throughout; the nearest approach to a typical instance is:—

Case 1.—This is from T. H., a man aged 42 (Sir W. Gowers), who had presented symptoms referable to the left Frontal region of eighteen months' duration. Unfortunately the operation notes have been mislaid, and one can only find that the left Frontal region was explored (Sir V. Horsley), and some part of the tumour removed, from which this section was made. The patient died at home not very long after, but the reply is very indefinite. (Fig. 1.)

The noteworthy histological features (fig. 1) are[1]:—

(1) A fine, loose-meshed glia reticulum.

(2) Delicately stained, barely visible glia-cells, with three or more branching processes, which divide into a fine reticulum which forms the stroma or connective tissue basis of the tumour. To show these elements a counter-stain, such as Van Gieson's, is necessary.

(3) Scattered over the section in not excessive numbers are the glia-nuclei, always deeply stained by hæmatoxylin. I call these "glia-

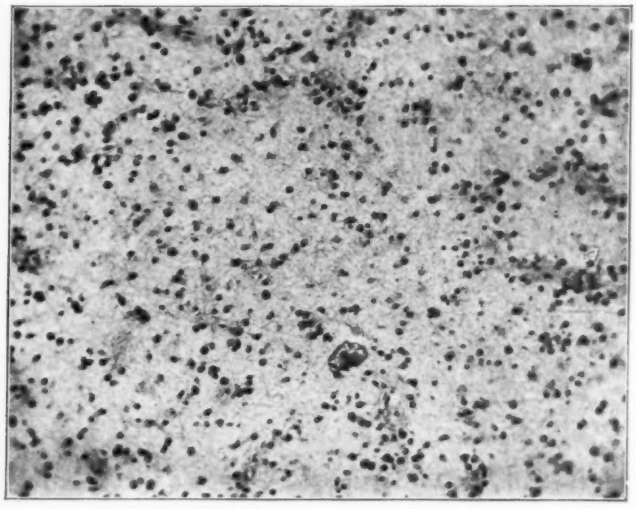

FIG. 1.—Case 1. Section of a glioma of a low degree of malignancy. Frequent arrangement of nuclei in circles or semicircles of very varying diameters, also in places in almost straight lines.

nuclei" to distinguish them from the more histologically definite "glia-cells." Possibly they also are cells with an invisible cytoplasm. The term is provisional only. They should be fairly uniform as to size and not grouped, but even in this apparently innocent quiescent picture these cells tend to show an arrangement in circles or segments of circles, a feature to be referred to later when considering the more malignant types.

(4) The blood-vessels are few and their walls lined internally by a single layer of flattened endothelial cells.

[1] In preparing the photomicrographs throughout a Zeiss D. objective has been used without correction. This has the advantage of giving sufficient magnification, without requiring great illumination, but at the expense of complete flatness of field.

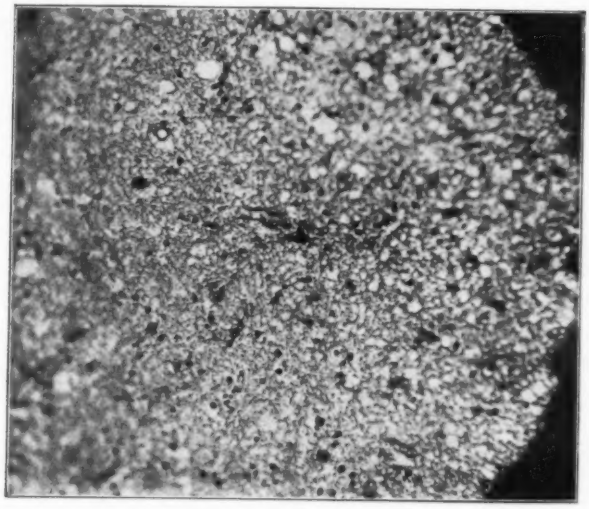

FIG. 2.—Case 2. Quiescent glioma. Very few glia-nuclei. Some cyst formation. (Section not flat.)

FIG. 3.—Case 2. From another part of the same tumour as fig. 2. Hæmorrhages in the centre of the field.

These are the characteristic features of the simple (?) non-malignant phase of a glioma.

There is reason to suppose that a glioma may retain these apparently innocent characters for an indefinite period; in fact, the clinical history of many cases can be explained in no other way. It is conceivable that in such a phase the growth may be no more malignant than a lipoma. Moreover, rarely, it may be removed successfully without recurrence.

In confirmation of this statement is the following case :—

Case 2.—A girl, E. B., aged 19 (Dr. Bastian), admitted in 1904 with marked clinical evidence of cerebellar tumour. First symptom one and a half years before. Operation (Sir V. Horsley) disclosed a tumour the size of a hen's egg, occupying the left lobe, vermis, and part of the right lobe, which was removed. The patient is still alive, eight years after, and in excellent health. There is no bulging of the wound, so probably no tendency to recurrence. But owing, no doubt, to considerable permanent destruction of cerebellar tissue, she still presents many of the symptoms—ataxia and paresis of the legs—of a cerebellar lesion. She is so well that she is about to join her father in Canada. (Figs. 2 and 3.)

Sections of the tumour removed (figs. 2 and 3) show a rather thickly felted stroma, so much so as to hide the glia-cells; small cavities are seen all over the section, indicating cyst formation so common in all gliomas. The glia-nuclei are relatively few, another suggestion of quiescence. Hæmorrhages may be seen, but possibly these may be due to operative manipulation.

Unfortunately this is a rare result, much too often the sequel is recurrence.

Now, assuming that there is such a thing as an innocent, latent, quiescent glioma, in what elements of the growth do the changes occur which constitute malignity, and what are those changes? The physiological process in action would appear to be that of active proliferation; this has its seat in: (1) The normal glia-nuclei of the stroma; (2) the glia-cells; (3) the blood-vessels.

(1) *The nuclei.*—The number of these may be variable within limits which may justify our considering the appearance as of an innocent type. But one evidence that these nuclei may be sharing in the awakening of proliferative activity is their arrangement into circles or even lines, as has already been hinted in fig. 1. To what extent they share in the ultimate richly nucleated and cellular growth of the malignant glioma I am unable to say.

(3) *The glia-cells.*—The evidence that the glia-cells play a most, if

not the most, important part in malignant activity seems to be quite clear. The alteration from the normal consists in: (*a*) Enlargement of the glia-cells; (*b*) increase in their number, though still retaining their morphological character, dendritic processes for instance; (*c*) multiplication of their nuclei; dislocation of these to the periphery of the swollen cell; (*d*) disappearance of the original cell, and independent existence of nuclei, which now resemble round sarcoma cells in a state of active multiplication.

This, I think, must be the sequence of events in many, if not all, of the malignant types. But it is possible that new cells, having some resemblance to altered glia-cells, may have a different origin, and the resulting growth may then more nearly resemble a true large-celled sarcoma. This is a difficult point, and it may be that the glia-nuclei may bear a larger share in this process than has been suggested above. It must not be forgotten that all these changes, in varying degree, may be seen going on in the same growth.

In illustration of the foregoing remarks are the following cases:—

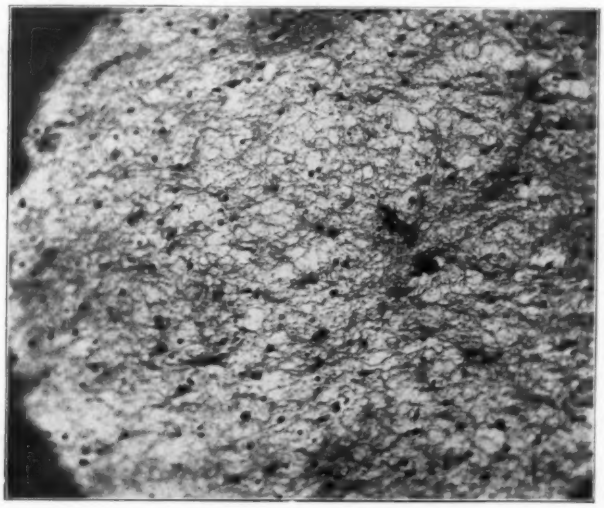

FIG. 4.—Case 3. Glioma of innocent appearance. Glia-nuclei small and few. Glia-cells difficult to see; one large one to right of centre.

Case 3.—A man, W. E. T., aged 50 (Dr. Buzzard); symptoms of ten months' duration. A fit followed by right hemiplegia and partial aphasia.

Operation (Sir V. Horsley), left Central, discovered a large subcortical tumour, a cyst the size of a hen's egg, was drained, and part of the wall excised, from which the section was taken. A considerable hernia resulted, and later sepsis showed itself. Five weeks after, another operation was performed, but the notes are here defective. A febrile condition set in; he became quite aphasic, and died three months after admission. (Figs. 3, 4, 5, 6.)

Fig. 4 shows a simple, sparsely nucleated, somewhat cystic reticular stroma with only one doubtful glia-cell in the field. No evidence of active growth.

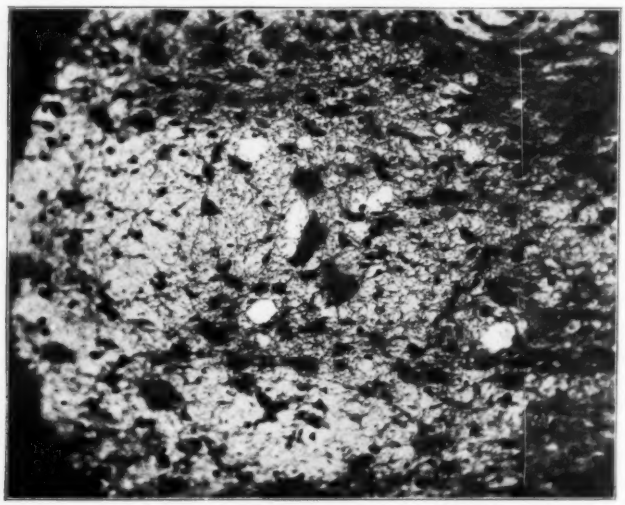

FIG. 5.—Case 3. Evidence of activity. Glia-cells enlarging, their nuclei multiplying, shown in two cells in centre of field.

Fig. 5, the same stroma, but a considerable, not excessive, number of large glia-cells variable in size, some containing more than one nucleus. Glia-nuclei more abundant. General appearance of activity.

Fig. 6 from another part of the section; the stroma is more condensed, and glia-nuclei are in greater abundance than in the last two fields. The glia-cells are also here in some number, and of very variable size. Their proliferated nuclei are situated in rings round the periphery of the smaller cells; in places these rings are all that remain.

Case 4.—T. W. A., a man, aged 47 (Dr. Taylor); symptoms dated only fifteen weeks before admission; paræsthesia of the left arm and leg in attacks

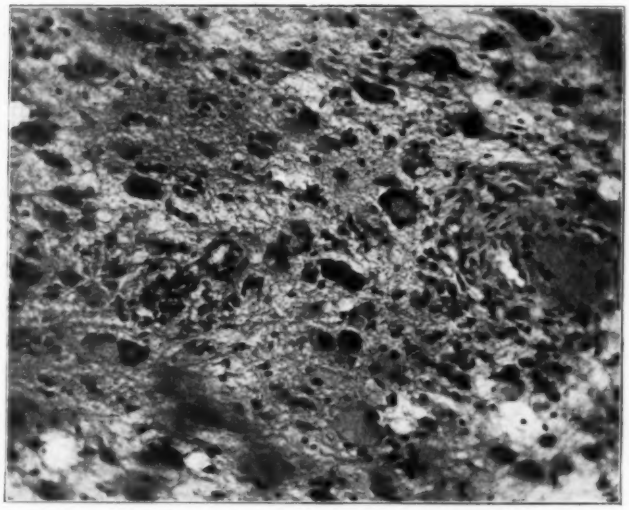

FIG. 6.—Case 3. From a more active part of the same glioma as figs. 4 and 5. Proliferation of nuclei of glia-cells, disappearance of cells, leaving rings of nuclei.

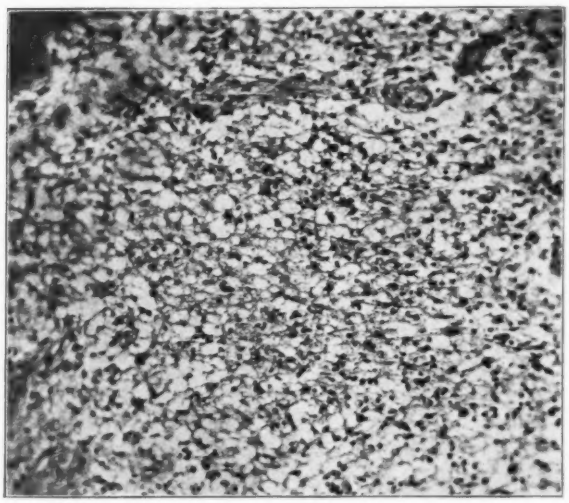

FIG. 7.—Case 4. Glioma. Stroma finely reticular and cystic. Nuclei small, but in considerable numbers. Glia-cells of normal appearance and number.

of three months' duration. Left hemiparesis and anæsthesia on admission. Double optic neuritis and left hemianopsia. Operation (Sir V. Horsley) four days after admission. Right Parieto-temporal not much bulging at first stage, but this was more evident at the second five days after. A large tumour subcortical to the right post-central region was found extending to the descending horn of the lateral ventricle, forward to the lower part of the precentral convolution, and back to the supra-marginal region. It was removed as far as possible. The patient made a fair recovery, but considerable bulging resulted, and there remained a left spastic hemiplegia. I hear from his wife that he died five and a half months after operation outside the hospital. (Figs. 7, 8, 9.)

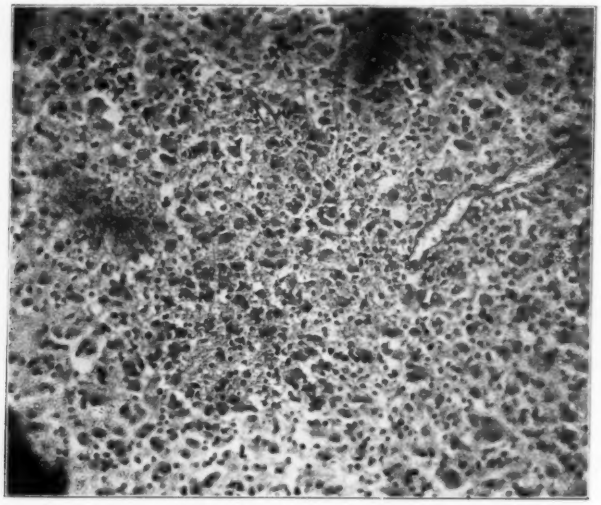

FIG. 8.—From same as fig. 7. Richly cellular, but glia-stroma retained. Cells mostly oval with a nucleus at one pole.

Fig. 7 shows a fine specimen of the simple type of glioma. The glia-nuclei are fairly abundant, but small, and with little evidence of proliferation. The stroma, however, has a cystic appearance, and the glia-cells are few and of normal character.

Fig. 8.—Here is a centre of activity, many definite cells of various size, some possessing glia-cell characteristics, others barely recognizable as such. Some with more than one nucleus, others with only one, but at one pole of the cell. I am doubtful of the true interpretation of this appearance, which is a common one. The cells are almost too small for

swollen glia-cells, they are mostly uni-nuclear. They may be swollen "glia-nuclei" and not glia-cells. Here and there the tendency to ring arrangement of nuclei is also to be seen in places.

Fig. 9.—In another part of the section is an area of necrotic degeneration, and in the neighbourhood of these areas one repeatedly finds thrombosed vessels; this will be referred to later.

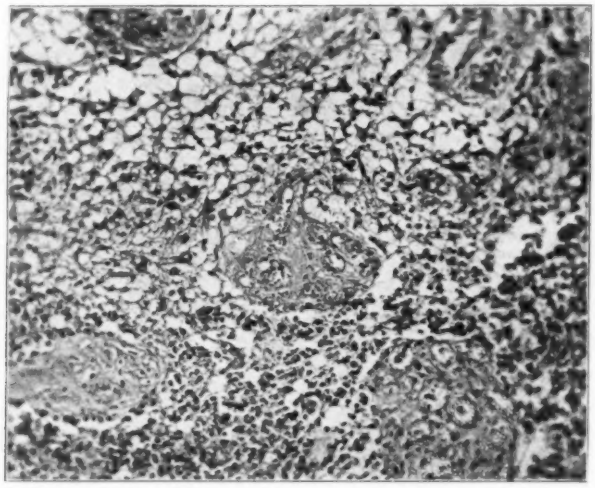

FIG. 9.—Case 4. Vessels thrombosed, on the border of an area of necrosis. Lower half of section.

Case 5.—T. J., a man, aged 38 (Sir W. Gowers), was admitted in March, 1904, with a seven months' history of failing memory, fits, development of the dull, lethargic mental state of a frontal tumour, and intense double optic neuritis. A month after admission the right frontal region was explored (Sir V. Horsley), and a cystic tumour was found presenting as a small patch 1 in. in diameter in the middle of the right middle frontal convolution. On incision this proved to be the wall of a large cystic cavity; this was removed as much as possible, the area of removal reaching to the lateral ventricle. He made a good recovery, and left hospital, with some bulging of the wound, optic neuritis much subsided, and mental state natural, two months after. The hernia, mostly fluid, increased, and it was tapped with some relief three months after operation. The subsequent history of the case will be considered later under the head of "Recurrence." (Figs. 10 and 19.)

Fig. 10.—A section of the tumour removed at the first operation. The glia-stroma presents no greatly abnormal appearance, it is somewhat condensed and cystic, and the glia-nuclei are not excessive in number. But what I take to be the glia-cells are in great numbers, large and swollen, yet with in many instances their dendritic processes retained. In some the nucleus seems to have disappeared, in others it is displaced to one pole of the cell, or in others there is more than one. This seems to me a more convincing illustration of the part played by the glia-cells than any I have yet shown. In some parts these cells have multiplied to the extent of obscuring all the other features of the original glioma.

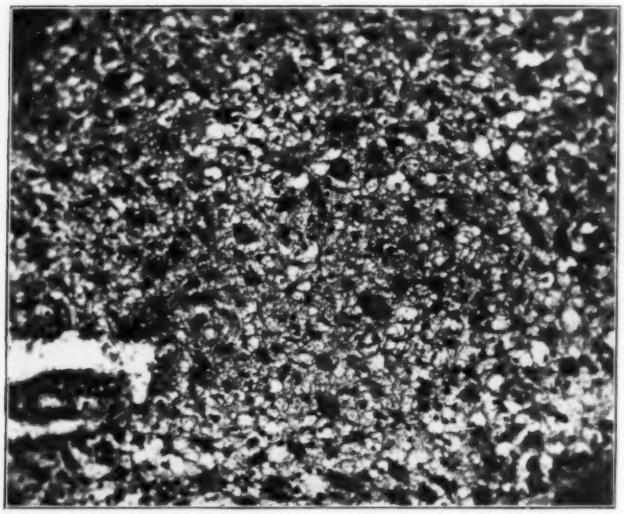

Fig. 10.—Case 5. General glia-cell enlargement and multiplication, suggesting considerable malignant activity. The cells retain their processes, many are still uni-nuclear, or devoid of nuclei. The stroma is denser than in the last case, and cyst spaces are numerous.

The following is yet another instance. In spite of the very malignant appearance of the growth, this patient is still alive.

Case 6.—F. B., a man, aged 35 (Sir W. Gowers), admitted July, 1908, with a six months' history of failing memory, faints, headache, vomiting, diplopia, and failing vision. His mental state, defective memory, "dreamy states," were suggestive of a Temporo-sphenoidal tumour, and two months after admission a large cystic tumour was removed (Mr. Armour) from the left Temporo-sphenoidal

lobe. After operation he was quite aphasic for a time, but this improved, so that four months after he could talk well and get about. But he remained emotionally unstable, and a large hernia cerebri developed. He was readmitted three years after operation with an enormous hernia. Mental condition vacant and stupid, memory and attention very poor. Right hemiplegia. Vision: right, blind; left, $\frac{6}{60}$. Optic disks: right, consecutive atrophy with + 4D. of swelling; left the same, but to a less degree. From the reply I have received I judge that he is in much the same condition, perhaps worse, than when last seen. (Figs. 11, 12, 13, 26.)

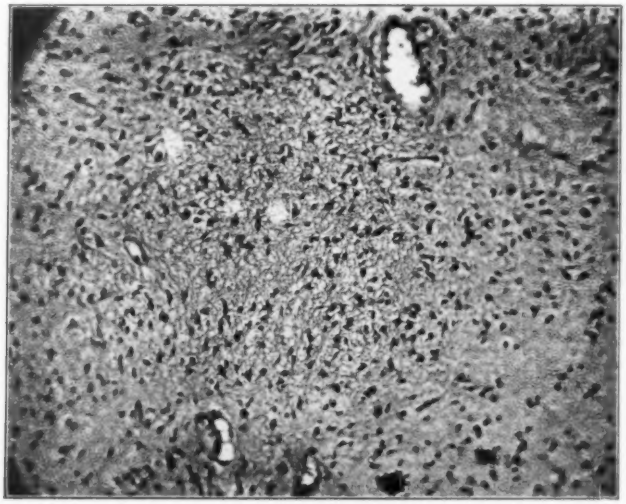

FIG. 11.—Case 6. Glioma. Stroma rather dense. Nuclei present a shrunken angular appearance. No marked evidence of activity.

Fig. 11.—All parts of the growth show some evidences of its gliomatous nature, and this part has almost an innocent appearance, but the glia-nuclei, if such they are, present an unusually angular appearance.

Fig. 12 shows a great multiplication of glia-cells, less convincingly glia-cells perhaps than in the last case, but still retaining in many of them the multipolar form, and more closely packed. Multi-nucleation is also well shown. But some of the cells are oval and uni-nuclear, as in fig. 8.

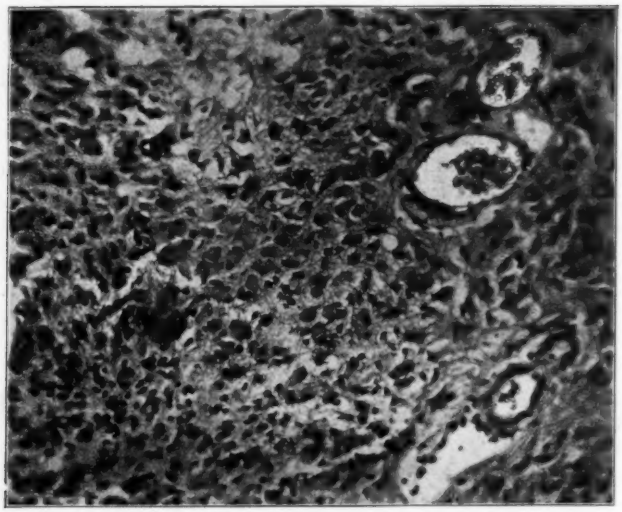

FIG. 12.—Case 6. From an active part of the growth. Many swollen multinucleated glia-cells. Some oval with single nuclei, as in fig. 8.

Fig. 13 shows the same characters considerably enlarged.

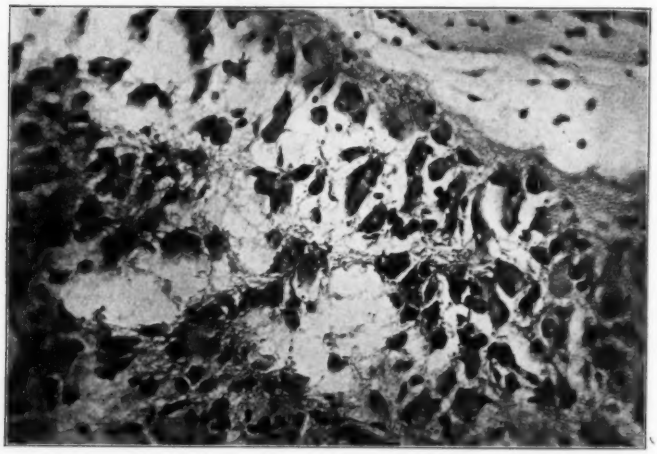

FIG. 13.—Case 6. The same appearances as in fig. 12 enlarged.

Case 7.—H. C., man, aged 31 (Sir W. Gowers). The first symptom, sudden failure of vision and memory, dates only six months before death. He presented the typical mental state of a frontal growth, disorientation in time and space, jocular mania "Witzelsucht," anosmia, double optic neuritis passing to atrophy, with great amblyopia. An operation was arranged for, but he died the day before, eight days after admission. This is one of the most rapid cases. *Post-mortem* a tumour was found involving the median and orbital surface of the left frontal lobe extending into the right. (Fig. 14.)

Fig. 14.—The field is packed with large cells of varying sizes, and containing one to six nuclei, generally peripherally disposed. The cells

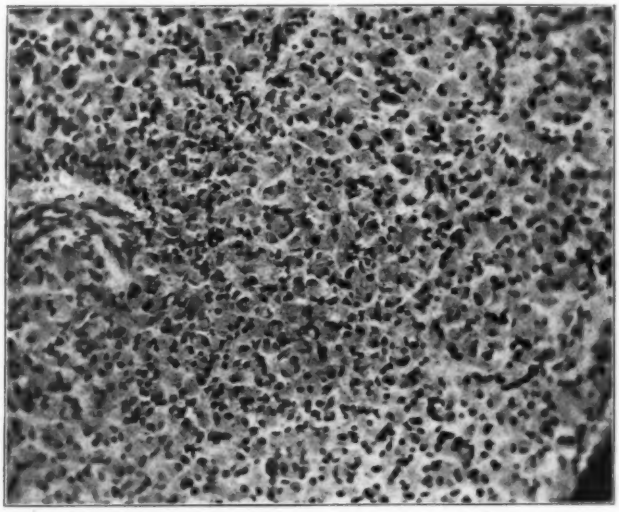

FIG. 14.—Case 7. Closely packed large cells; cytoplasm faintly stained; multinucleated; nuclei peripherally disposed. Disappearance of parent cell, leaving a ring of nuclei.

contain a faintly staining granular cytoplasm and some are angular, but the original glia-stroma is very little in evidence. The annular arrangement of the escaped nuclei is well seen and within their circles may be seen the remains of the parent cell. This picture I regard as the extreme result of glia-cell proliferation. If not viewed by the light of the preceding cases it might well be regarded as a large cell sarcoma.

Gliomas are not commonly multiple, and metastasis is almost non-existent. The following is a case of two tumours, one of which was a glioma and the other probably an angio-sarcoma.

Case 8.—W. E. G., aged 51 (Dr. Taylor). Another very rapid case, five months from first symptoms to death. He gave a history of left hemianopsia and rapidly failing vision to complete blindness. He was in hospital under a month, during which he became more and more stuporose and died. *Post-mortem* a large tumour was found occupying most of the right occipital and temporal lobes, and another small one was in the right marginal gyrus, about 1 in. in diameter, hard and deeply congested. (Figs. 15, 16, 22.)

Fig. 15 from the large occipital tumour is obviously a glioma. In spite of the rapid history this section shows little evidence of great

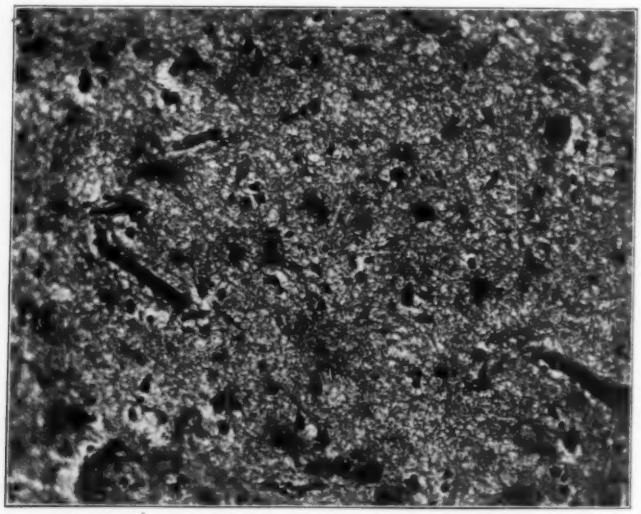

FIG. 15.—Case 8. Occipital glioma. A densely reticulated stroma with large and not very many glia-cells; a few glia-nuclei.

activity. Probably sections from other parts of the growth would discover appearances of malignancy similar to those in the preceding cases.

Fig. 16 is a spindle-celled growth with many vessels, an angio-sarcoma.

I do not suggest any pathological connexion between the two growths, but the case is interesting from its comparative rarity.

The next stage in this moving picture of proliferative growth that demands attention is that concerned in the further progress of the nuclei

liberated by the disappearance of the parent glioma-cells, by which an appearance is produced different from that hitherto described in this account.

Malignant activity is plain enough in some of the sections figured above, but to my mind it is still more so in the stage to which we have now arrived; in fact, the histological picture is that of forces suddenly brought to a standstill when in full play. In illustration of this—

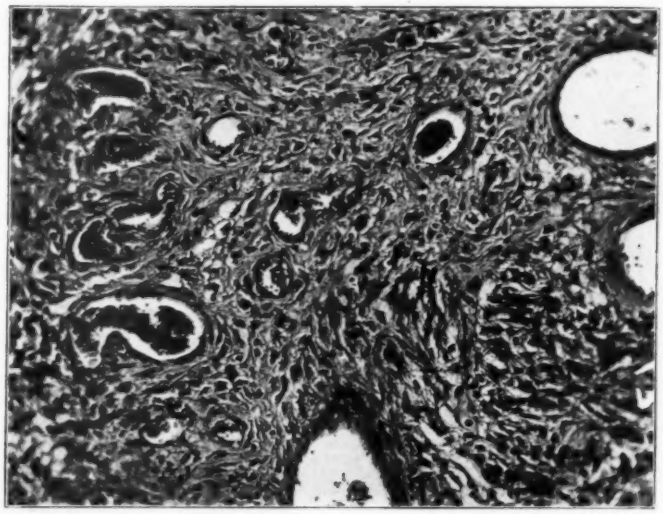

FIG. 16.—Case 8. Second small, hard, vascular tumour in straight marginal gyrus; an angio-sarcoma.

Case 9.—A. M., aged 37 (Dr. Beevor), admitted July 1, 1904, with a long history, two years, of fits, no details given; ten months, visual symptoms suggesting left hemianopsia, which was confirmed on admission; four months, fits beginning in the left foot. No hemiplegia, no optic neuritis. Readmitted in December, 1904, seven months afterwards; two months after this optic neuritis appeared, a post-central growth was diagnosed, and operation followed (Sir V. Horsley), February, 1905. A large cystic tumour, cyst within cyst, was shelled out. The patient made a good recovery and was discharged as "cured." He was readmitted in June, 1906, four months after operation, with progressive left hemiplegia and hemianæsthesia, but the optic disks were clear and showed no evidence of past neuritis. I heard from his widow that he died in September, 1906—i.e., nineteen months after operation. (Figs. 17 and 18.)

Fig. 17.—Section of the growth, which includes a piece of cortex, under which the growth lies. This is a cellular glioma, rich in large swollen cells, but with their processes yet retained, and some of the glia-stroma reticulum between, also rings of nuclei, many of small diameter, showing within their circumference the remains of the parent cell.

Farther away from the cortex the large cells are in still greater abundance, packed closely and also crowded with nuclei round about them.

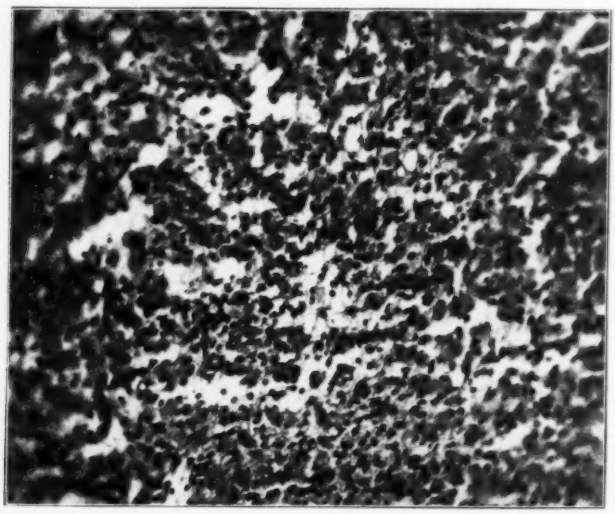

FIG. 17.—Case 9. Richly cellular and nuclear glioma. Of the large cells many are multinuclear, and many are disappearing, leaving a ring of nuclei.

Fig. 18.—Farther still we find the nuclear elements in such numbers as to obscure the parent cells or their remains, though by careful focusing many may be seen. The picture now is that of a small round-celled sarcoma, but by no effort of focusing can one see any cytoplasm surrounding these nuclei. Possibly recent special stains may show that these are the nuclei of new cells, but I have not yet had the opportunity of seeing the result of their use.

The arrangement of these nuclear elements of the growth is also characteristic; in all parts of the field are circles or half-circles, rarely straight lines, presumably in whatever plane the section is made. The circles may be small, no larger than the circumference of the parent

cells from which they come, but they show a tendency to an ever widening radius, suggesting lateral division of neighbouring nuclei. The semicircles of course suggest a slight tilting of the plane of that circle, so that half is in one section and the other half in the next above or below. So frequent are the rings in any given plane that one is tempted to conclude that every nucleus all over the field is one of a little circle of its own in another plane. This annulation, as representing independent centres of growth infinite in number, bring home to the mind of the observer the intensity of the exuberant activity that constitutes high malignancy. No doubt this annulation has been seen often enough by other observers, for it can be seen in all these richly cellular growths.

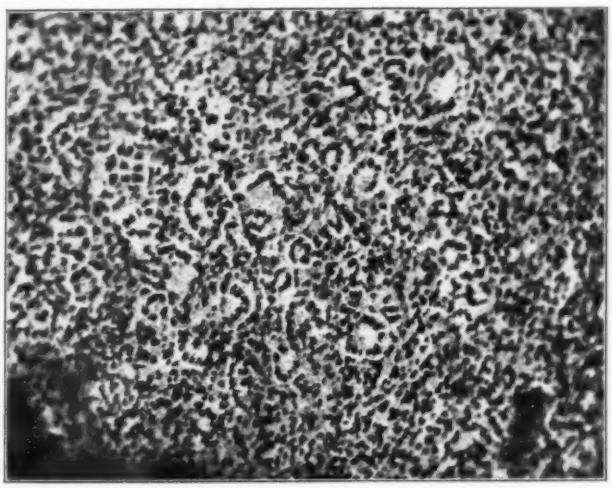

FIG. 18.—Case 9. Illustrating ring formation, or annulation. In a thick section underlying features tend to confuse a photograph; therefore in this figure some of the details immediately adjacent to the most obvious rings or semi-circles have been blocked out.

Annulation has been demonstated as occurring in a greater or less degree in many of the preceding figures. In fig. 1 even it is seen, and in this also can be seen the tendency to formation of straight lines, which may be a common arrangement, but it would naturally be less evident in a crowded picture. A similar grouping of nuclei may be seen in the growing brain (see the article on the "Cyto-architecture of the Cerebral Cortex," by Bolton and Moyes, in this volume of *Brain*, p. 14, fig. 7).

From the foregoing observations one seems to be justified in conceiving an ascending scale of malignity from the slow-growing or quiescent overgrowth of glia-tissue to an anatomical picture resembling grossly malignant sarcoma. These may be, and are, called glia-sarcoma, but I have avoided using the word; it seems unnecessary and perhaps misleading to have another word for what would appear to be a phase of growth only, if that is the right reading of these changes.

Recurrence.—In several cases an opportunity has been afforded of examining the growth removed by operation and subsequently the recurrent growth at a second operation, or *post-mortem*. The two cases following are the simplest, the others present such complicated appearances and would require so many photographs to bring out all their features that I have thought it wiser to omit them.

Case 5.—Sequel (*vide supra*, p. 87). Three months after removal of a large cystic frontal tumour a large resulting hernia was tapped with some relief. The histological appearances of the growth removed at operation are shown in fig. 10. He was readmitted five months after operation and stated that he had been practically well until six weeks before, since when he had had two to four fits a week and he became mentally dull and lethargic. He was in hospital for a month, and left much improved mentally but with a large fluid hernia as before. During stay in hospital he had one general convulsion. He was readmitted for the third time nine months after operation with a progressive left hemiplegia and much mental dulness and apathy. His condition not improving, the flap was reopened nine days after admission and a large quantity of clear fluid was found in a cavity, the site of the original tumour. At the bottom of this cavity a mass of growth was seen and removed. He did not recover consciousness and died the next day, the temperature rising to 104·8° F. (Fig. 19.)

Fig. 19 shows very similar appearances to those of the last case, fig. 18. No glia-cells can be seen at all. Annulation is quite distinct and there is no superficial resemblance to the original growth. It shows every appearance of rapid recurrence and would no doubt eventually have filled the cavity left by the old tumour.

Case 10.—This is a more doubtful illustration of recurrence than the last, because the time which elapsed between the removal of the growth and the *post-mortem* is so short, eleven days only. But the time element in pathological events is always an almost unknown factor.

W. O., a man, aged 42 (Dr. Batten), admitted November 4, 1910, with an eighteen months' history of frontal headache and frequent faints, eight months failing vision and memory, and slight sphincter weakness. He showed some of the mental symptoms of frontal tumour, which became more definite later, and intense optic neuritis and swelling, rather more pronounced on the right side.

Twenty-five days after admission the right frontal region was explored by

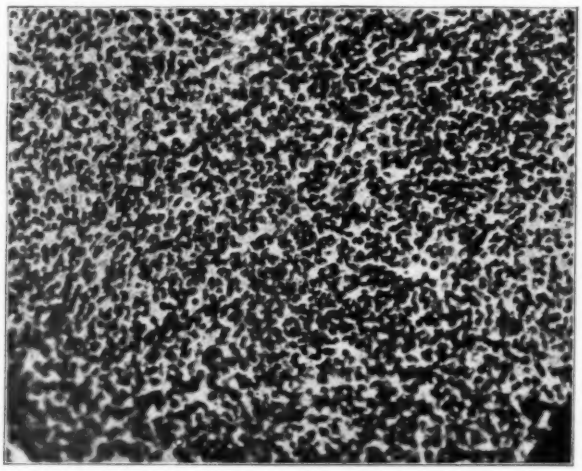

FIG. 19.—Case 5. Section of mass of recurrent growth, resembling closely fig. 18. Annulation is obvious, also a tendency to arrangement in lines more or less straight.

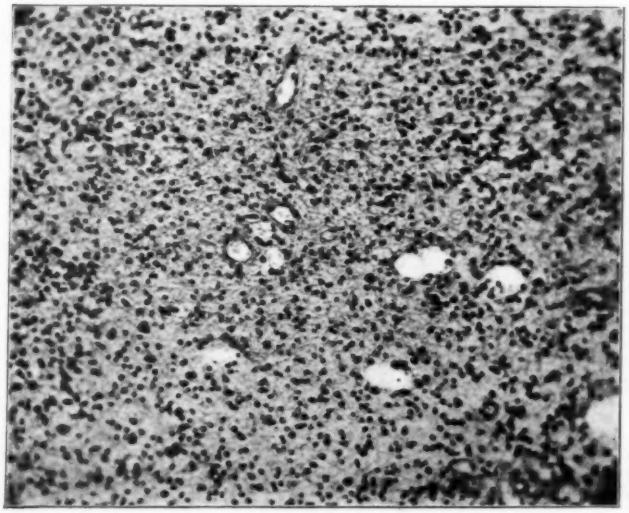

FIG. 20.—Case 10. From the glioma removed at the second operation (the first was exploratory). The stroma is finely and normally reticular, and the glia-cells few and almost invisible. But the nuclei are in great number, and annulation well shown all over the field. Two normal vessels are seen on each side of an annulus, to the left of the centre.

incision (Sir V. Horsley); the substance was thought to be abnormally firm and nothing was done. The patient made a good recovery and the neuritis subsided rapidly. He was discharged to the Convalescent Home, but was readmitted four months after operation, with headache again, mentally emotional and slow cerebration. There was an increasing hernia, and a renewal of the optic disk swelling. Another operation was then performed. On exposing the frontal lobe a large cyst burst, which was partly removed. There was no relief this time, the temperature fluctuated between 100° and 104° F., and patient died eleven days after. At the autopsy the main tumour was found in the mesial side of the right frontal lobe extending over to the same side of the left frontal and forward to within 1 cm. of the frontal pole and back to the anterior horn of the lateral ventricle, involving the genu of the corpus callosum, from which it may have originated. (Figs. 20 and 21.)

Fig. 20.—A section of the tumour removed eleven days before death is a fine example of a glioma in which the glia-cells seem to be little affected. The reticular stroma also is fairly normal and also the vessels. But the field is richly nucleated and annulation is evident. The nuclei are variable in size and in places still more numerous than in this figure. This is a good example in illustration of a probable share taken in proliferation by the simple glia-nuclei.

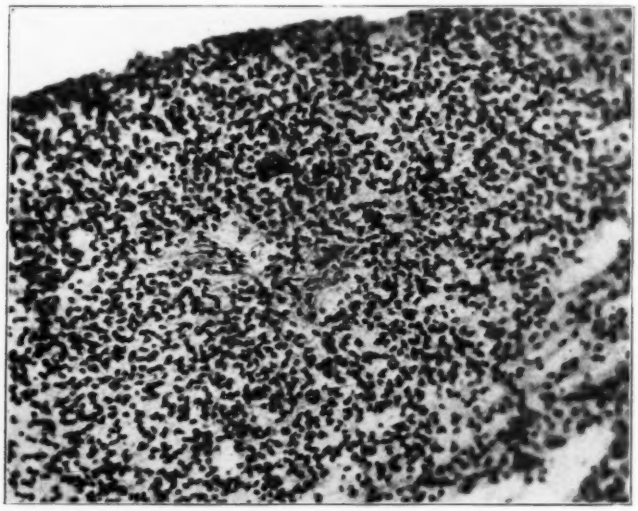

FIG. 21.—Case 10. Recurrence. From the growth removed (*post-mortem*) eleven days after the second operation. The appearances are almost exactly similar to those of fig. 19.

Fig. 21.—A section of the growth removed *post-mortem*. Unfortunately most of the section is of altered brain substance, but there is one portion of it sharply delimited, and evidently growth which resembles in every respect the recurrent growth of the last case; little if any glia-stroma is to be seen, but somewhat irregular annulation is visible all over the field.

If these appearances are to be accepted, and I offer them with the greatest possible diffidence, one is forced to infer, on pathological grounds alone, that surgical interference, exploration, or manipulation, with few notable exceptions, is liable to awake into greater activity a tendency to exuberance which perhaps may be almost latent at the time.

The Rôle of the Blood-vessels.

What part do the blood-vessels play in the growth and progress of the glioma?

In vascularity these growths show wide variations, from one or two small thin-walled vessels to the field, of which the endothelial lining is marked by a few nuclei at regular intervals, to the development of numbers resembling an angioma.

The larger vessels should present the natural appearance of an arteriole, but sometimes one finds, especially in the more angiomatous forms, a thickening and condensation of the glia-tissue round about the large vessels as in fig. 22, belonging to Case 8, in which the second tumour was an angio-sarcoma.

But in many cases the small vessels show great swelling and proliferation of the endothelial intima. Fig. 23 is from another case of recurrence after removal. The recurrent growth was more vascular than in the cases above mentioned, and the stroma presents a fibro-sarcomatous appearance, which was absent in the original growth. This section illustrates the swelling and proliferation of the endothelial intima. The vessel may remain pervious, but if the process continues the ultimate result is complete blocking of the lumen and a picture that is almost unrecognizable as a vessel at all may result.

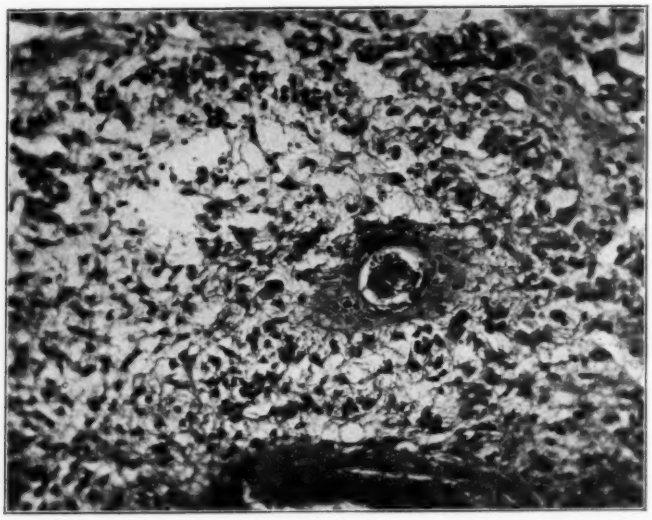

FIG. 22.—Case 8. Detail from the smaller tumour, of which fig. 16 gives the general characteristics of angio-sarcoma. A vessel surrounded by condensed, almost fibrous tissue. In this particular situation the stroma somewhat resembles that of coarse glioma, but it is exceptional, and probably a necrotic effect.

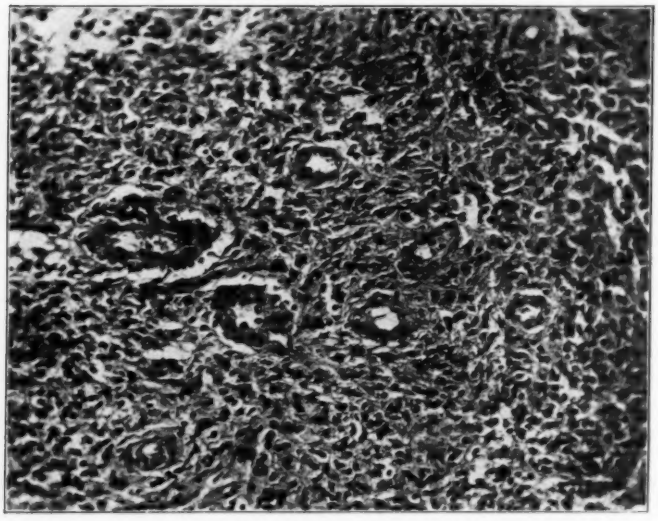

FIG. 23.—From a recurrent growth after removal of the original tumour from the post-central area. The small vessels show swelling and proliferation of the intimal endothelium, but many are still pervious.

FIG. 24.—Case 11. From a large glioma of the centrum ovale. Great vascularity, but intimal proliferation is not shown in this section.

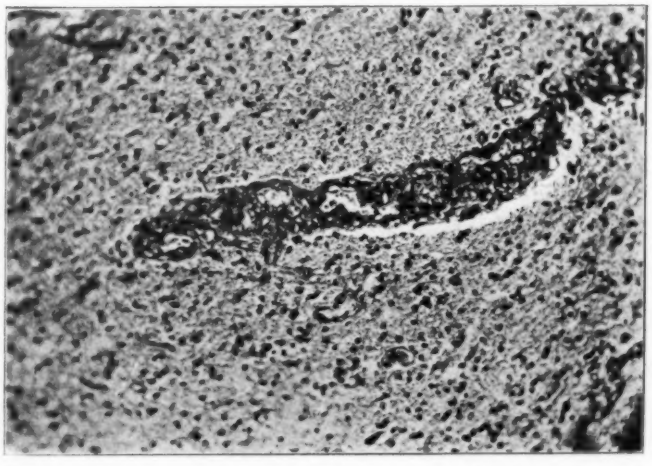

FIG. 25.—Case 11. A longitudinal section of a vessel, showing an extreme effect of endothelial proliferation.

Case 11.—H. B. (Dr. Tooth), a large glioma of the right centrum ovale. The patient died seven years after the first symptom. (Figs 24 and 25.)

In places (fig. 24) the angioma formation only is seen. In others the intimal proliferation is very striking (fig. 25). A similar instance is taken from Case 6 (fig. 26).

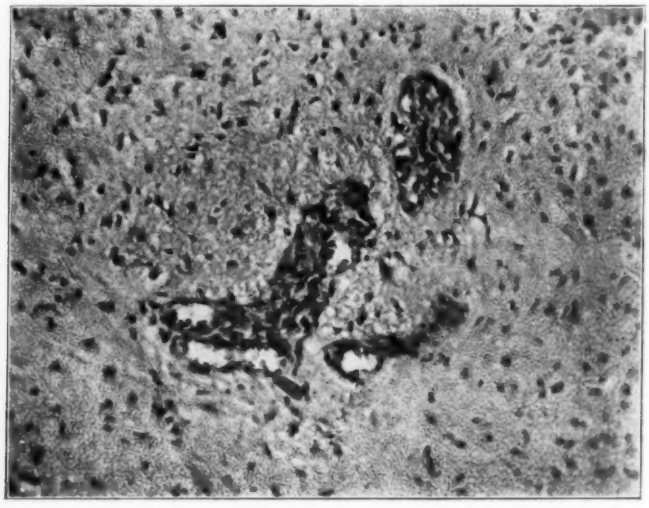

FIG. 26.—Case 6 (*vide supra*). A longitudinal and almost transverse section of (?) the same vessel. Showing complete obstruction of the lumen.

The following illustrates some of the features of vascular change very well.

Case 12.—W. H., a man, aged 47 (Dr. Jackson). Two months before admission he fell on the back of his head and immediately after his left leg became weak and this progressed. The connexion between the blow and the onset is so obvious that one must suppose that the tumour was in existence in a latent form and that traumatic influences either woke up malignant activity or caused a small hæmorrhage. However that may be, the case ran a rapid course from this time, and a left hemiplegia with gross optic neuritis resulted. Two months after the first symptoms he came to operation and the arm-area was found involved in growth, a richly cellular glioma of ill-defined margin extending deeply to the lateral ventricle; as much as possible was removed. He made a good recovery, and all symptoms improved; hemiplegia less, and optic neuritis subsiding. He wrote four weeks after discharge that he was still improving, but I learn that he died later, ten months after the first symptom. (Figs. 27, 28, 29, 30, 31.)

Fig. 27 shows an intensely richly nuclear part of the growth; annulation marks its activity. Tiny vessels can be seen ramifying in all directions. They are quite primitive, little more than channels with a thin limiting membrane and no endothelium can be seen.

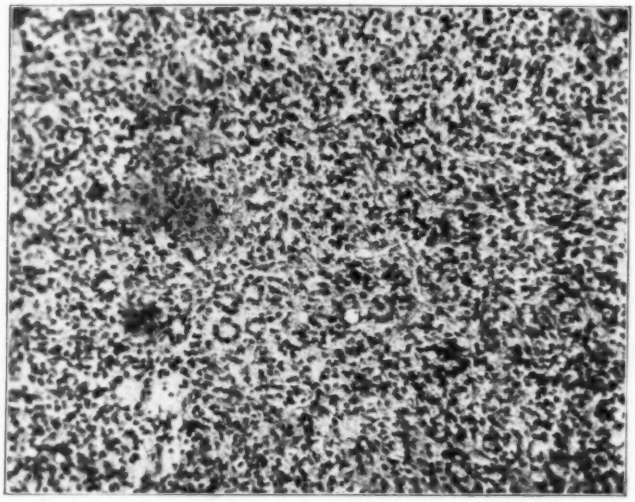

FIG. 27.—Case 12. From a highly active part of the growth. Fine vascular channels can be seen with a glass in the right central part of the field.

Fig. 28.—On the border of an area of necrosis; the small vessels are in great plenty, as indeed they are everywhere in all the sections, and the intimal proliferation can be seen in all degrees from the single layer of swollen cells to complete blocking of the lumen. The photograph is wanting in distinctness on this point.

Fig. 29 shows two bunches of vessels somewhat like a renal glomerulus. Some of the constituent vessels are pervious, and many are blocked.

Fig. 30.—In a necrosed area, a large vessel in the centre of the field, pervious, and containing blood corpuscles. Its wall presents a meshed appearance, which may be due to necrosis of proliferated intima, very much resembling on a small scale the structureless meshwork of a cholesteatoma. A neighbouring vessel appears to be thrombosed, full of fibrinous fibrils.

Fig. 31.—A vessel on the border of a necrosed area, probably containing organized thrombus.

In some of these pictures it is difficult to say how much the appearance is due to intimal proliferation—because the endothelium tends to degenerate with the other elements of the growth—and how much is due to organized clot. Both may be present; probably the sequence of events is—blocking of the smaller vessels which have an endothelial lining, by the multiplication of the cells composing it, and a subsequent thrombosis backwards to the larger vessels, and so starvation of blood to an area of the tumour.

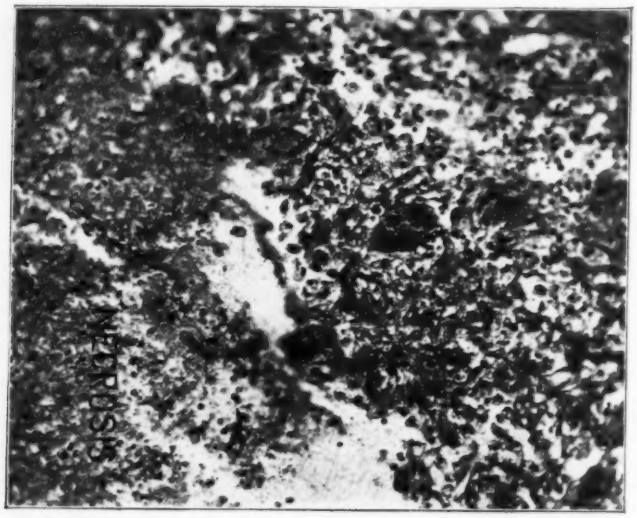

FIG. 28.—Case 12. Vessels on the border of an area of necrosis (left half of section). The central right half of the field shows a group of small vessels the endothelium of which is proliferated; but the photograph fails to bring out their features owing to obtrusion of other nuclear details.

Necrosis.—This brings us to the last stage in the life-history of the glioma—necrosis, a process which is going on *pari passu* with vigorous vitality elsewhere in the growth. Moreover, it is not too much to say that the more evidence existing in a given tumour of active growth, the more certainly will be found parts in which necrosis is in progress. Fig. 32 is a good picture of such an area taken from another case. There is an appearance of the calm of death about it—dissolution rather. The last remaining nuclei have still some chromatin, but it is fast disappearing; so they present a shrunken appearance very

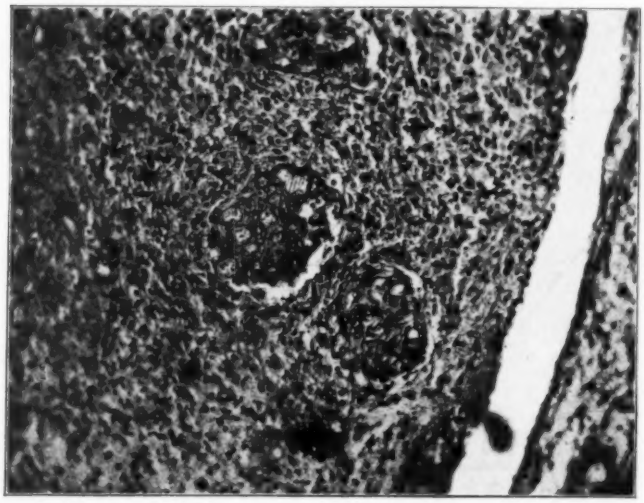

FIG. 29.—Case 12. Glomerular multiplication of vessels on the border of an area of necrosis.

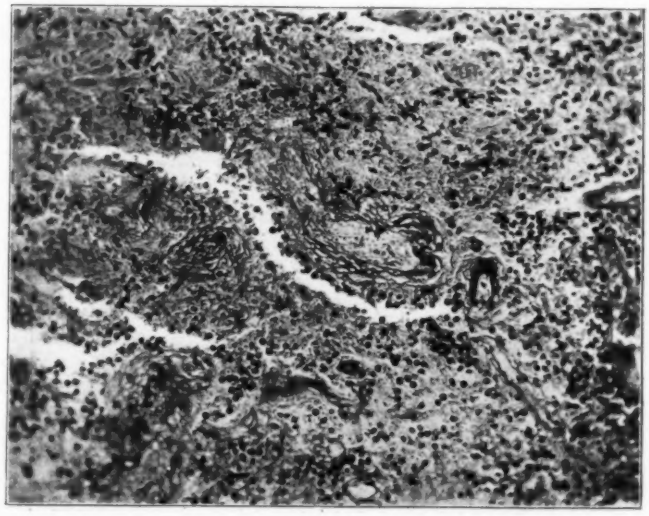

FIG. 30.—Case 12. In a necrosed area. In the centre of the field is a large vessel, pervious, containing blood. Its wall is meshed by degeneration. To the left is another in the same condition but probably thrombosed.

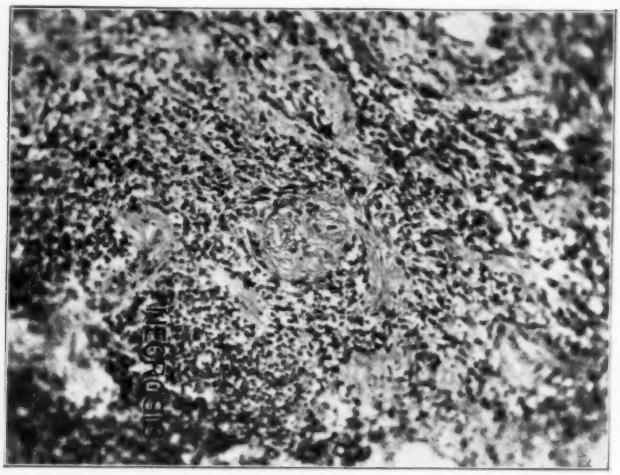

FIG. 31.—Case 12. A vessel on the border of a necrosed area. The appearance may be produced by organized thrombus.

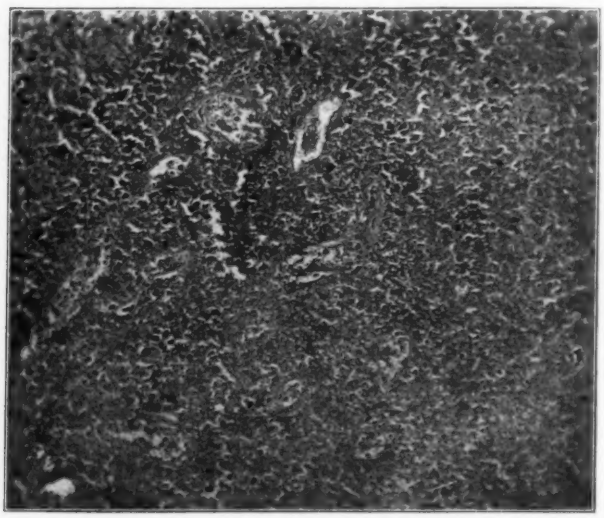

FIG. 32.—Necrosis. Granular amorphous ground substance with only a few nuclei remaining undergoing chromolysis.

different from the full, round bodies shown in so many of the active growths above. The rest of the field is made up of feebly staining amorphous débris, with here and there the remains of a blood-vessel also bearing evidence of decay.

Cyst formation.—The glioma shows the tendency to cyst formation perhaps more often than any other group. Pathologically this may be considered as a degenerative process, but clinically it may be as disastrous as the more malignant forms. Glioma cysts, which are sometimes single but more often multiple, may certainly be drained with temporary and even prolonged benefit, but it is doubtful whether the growth of the surrounding or underlying tumour, if of the active kind, is modified to any extent, and there is always the fear that by interference latency may awake to activity. This is, however, a risk that must be taken, in the event of operation disclosing an obvious cyst.

The simplest and earliest evidence of cystic tendency is shown in the rarefaction of the glia-stroma which may be seen in so many apparently innocent-looking growths. In its full development it presents a superficial resemblance to an emphysematous lung.

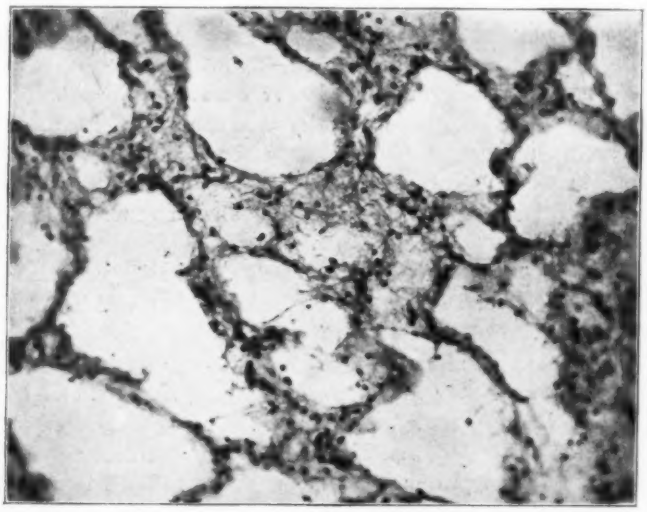

FIG. 33.—Case 13. Cyst formation, in a glioma of long duration. The glioma tissue presents no appearance of activity.

THE PATHS OF ENCEPHALIC INFECTION IN OTITIS.

BY CHRISTOPHER TYLOR, M.D.

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INTRODUCTION.

THIS paper has for its object the investigation of the various pathways by which infective processes, originating in the ear in the human subject, may reach the interior of the cranium.

The inquiry has been approached from the standpoint of the human morbid anatomist by a study of the *post-mortem* records of 644 cases of intracephalic infection, including 267 of infective diseases of the ear. Particular attention has been directed to those cases in which actual

Case 13.—E. W. H., a man, aged 30 (Dr. Ormerod), gave a long history commencing with a fit, general convulsions, three years before admission, general drowsiness a year before that; but the fit has been reckoned as the first symptom—sixteen months, vomiting attacks, two months, weakness right leg. Vision: right, $\frac{6}{36}$; left, $\frac{6}{9}$. Consecutive atrophy of the right optic disk and intense neuritis of the left. A frontal growth of a quiescent type was suspected. He improved in hospital, and was discharged to report progress later. He died one year after. Dr. Stewart made a *post-mortem* examination outside, and found a large right frontal tumour and a small left frontal, one of the few multiple gliomata. (Fig. 33.)

Fig. 33.—The cysts occur in the midst of simple glioma structure and the section shows no evidence of malignity; but of course if cysts continue to enlarge by increase of their fluid contents, such a growth, however innocent pathologically, is clinically malignant from simple mechanical increase in bulk.

Cyst formation, in fact, would appear to be an evidence of long life, from the pathological standpoint, and the process rather one of atrophy than of activity.

In conclusion, it is evident that the glioma, when it enters upon an active stage, by the very exuberance of its activity carries on within itself a process of self-immolation. Also that this aspect of the question centres round the blood-vessels, which may increase vastly in number—an angiomatous stage; become blocked—an intimal proliferative stage; thrombosis spreads backwards into larger vessels—a thrombotic stage; and lastly there results necrosis of the area concerned. If this is the true sequence and proper interpretation there may be some hope of treatment in the future by some application of ultra rays after removal of the bone, such as has given results in some other vascular growths.

But this is only one side of the matter. The larger question still remains, how to meet the forces that are seething within the rapidly growing tumour. Complete recovery of the diffuse forms is practically impossible. One may almost assume that the earliest possible stage of growth, when the tumour might conceivably be removed completely, is undiagnosable in most parts of the brain. A removal as complete as possible seems to be followed by increased activity, and recurrence, or, worse still, a relatively latent growth, may be awakened into malignity. It seems that in the present state of our knowledge we must be content with relieving pressure by decompression in all gliomata, lest worse befall.

branes are chiefly involved—the purulent form generally affecting a large area of the brain—which is usually in a condition of encephalitis.

(*e*) Serous meningitis and internal hydrocephalus.

(*f*) Tuberculous meningitis concomitant with infective disease of the middle ear.

The investigation has been conducted with the object of ascertaining, first, the most common situations of the different intracranial lesions, and, secondly, the paths whereby the infective micro-organisms have been enabled to gain access to intracranial structures.

The pathology of the various morbid processes, as far as it concerns the subject of this paper, will be discussed, as well as certain anatomical features which have an important bearing upon the paths of encephalic infection.

§ 1.—*Bacteriology.*

Micro-organisms can readily make their way from the nasopharynx viâ the Eustachian tube to reach the tympanic cavity, in the mucous membrane of which they proceed to multiply and to produce their toxins. Acute otitis media is a common complication of those acute specific fevers in which sore throat is a prominent feature (of which scarlet fever is perhaps the best example), and in these cases infection reaches the ear through the Eustachian tube. In other cases, such as tubercle, infection may be carried to the ear by the blood-stream. Again, many cases of meningococcal cerebrospinal meningitis are associated with otitis media. What relation the infection of the ear bears to the meningitis in these cases we have yet to learn.

In only a comparatively few cases have the specific organisms concerned been recorded; in the majority of cases no bacteriological examination of the infective material appears to have been made. In forty-nine cases a bacteriological report on the nature of the infecting micro-organism was given, and the results are set out in the following table :—

Organisms concerned in Forty-nine Cases of Infective Middle-ear Disease.

Source from which cultivations were made	Pneumo-cocci	Meningo-cocci	Staphylo-cocci	Strepto-cocci	Mixed infection diplo- and strepto-cocci
Pus in meningeal exudate	20	6	2	5	1
Blood	3	—	—	—	—
Pus in ear or mastoid	2	1	1	1	—
Pus from brain abscess	1	—	—	2	—
Pus from extradural abscess	2	—	—	—	1
Pus from labyrinth	—	—	—	1	—
Totals	28	7	3	9	2

post-mortem examination has demonstrated the origin and spread of infection, or in which the infective processes had been observed during life in the course of operative procedures.

In a survey of the *post-mortem* examination records of St. Bartholomew's Hospital during the last fourteen years, namely, from October 1895, to October, 1909, the total number of cases in which infective middle-ear disease occurred was found to be 267 (collected from both medical and surgical *post-mortem* registers). The importance of infective disease of the ear as a cause of intracranial suppuration has long been recognized, and in the series of cases collected for the purposes of this inquiry it was found that leptomeningitis, including the tuberculous form, accounted for a fatal termination in 644 cases, and of these middle-ear disease was present in 129 cases, that is, in 20·03 per cent.

It is only in recent years that the importance of the labyrinth in relation to intracranial disease has been recognized. In a surprising number of this series of cases it will be shown that infection of the labyrinth has been the antecedent of meningeal or encephalic infection.

As we might expect, in records of the earlier cases, it is not always possible to ascertain the paths of infection owing to insufficient details in the *post-mortem* reports, yet, in a good many instances in which direct evidence was wanting, the path of infection could be inferred with considerable certainty. These doubtful cases have been noted and classified separately.

Among the more recent *post-mortem* examinations, histological examinations of the labyrinth have been undertaken, and these have revealed inflammatory disease in a number of cases where it had not been suspected to exist.

The chief forms of intracranial infections met with are:—

(1) Lateral sinus thrombosis.

(2) Brain abscess, including both cerebral and cerebellar abscess.

(3) The various forms of meningeal infection. Of this latter class the following varieties will be considered:—

(*a*) Pachymeningitis, in which the dura mater and, more especially, its external surface (pachymeningitis externa) is alone affected.

(*b*) Extradural abscess, in which a collection of pus forms between the dura mater and bone.

(*c*) Intradural abscess, in which the pus is situated between the dura mater and arachnoid, and is limited to one particular spot by adhesions between the membranes.

(*d*) Purulent leptomeningitis, in which pia and arachnoid mem-

From the above table it will be seen that in the forty-nine cases in which a report on the nature of the infecting organism was made, the pneumococcus occurred in more than half, viz., twenty-eight; streptococci were responsible for nine, and meningococci for seven.

Bacteriological examination of the pus contained in the tympanum, or in those intracranial lesions secondary to ear-disease in cases of chronic infective otitis media for the purpose of ascertaining the organism primarily responsible for the disease, is of little value since the pus is almost certain to be contaminated by one or more organisms which have given rise to a secondary infection. The only satisfactory way of isolating the infecting organism is to examine bacteriologically the fluid from the tympanic cavity, obtained by aseptic puncture of the bulging tympanic membrane in the early stages of acute otitis media, or by examining the pus in acute mastoid abscess.

West [15], in the *St. Bartholomew's Hospital Reports*, gives the results obtained by him in an investigation conducted for the purpose of determining the organisms primarily concerned in the production of acute otitis media and consecutive suppurative mastoiditis. In cultivations made from the pus in thirteen cases, he obtained a pure growth of streptococci in nine, and of pneumococci in four instances. He points out, however, that in cases in which otorrhœa has existed for some time, and also in cases of meningitis, lateral sinus thrombosis and extradural abscess complicating a long-standing aural discharge, a pure streptococcal culture may often be obtained while the aural discharge is full of saprophytic organisms and *Bacillus coli*. He collected from the literature 100 cases of primary acute otitis media in which the bacteriological examination was trustworthy, and of these: 48 were pneumococcal, 27 were streptococcal, and 25 were staphylococcal; also 115 cases of acute suppurative mastoiditis, in which 74 were streptococcal, 34 were pneumococcal, and 7 were staphylococcal. These figures show that the infecting organism in cases of acute otitis media and mastoiditis is, in the great majority of instances, either some form of streptococcus or else the pneumococcus.

In the nine cases of middle-ear disease complicating diphtheria and typhoid fever no report on the organism present in the ear was apparently made, but in one case, associated with parotid abscess, the ear discharge contained diphtheria bacilli as well as staphylococci.

The presence of tubercle bacilli was demonstrated in two of the cases of tuberculous otitis media, but no bacteriological examination was made in the other cases.

The micro-organisms, therefore, which appear to be of chief importance in connexion with otitis media and its cerebral complications, are those which grow in long or short chains, namely, the streptococci and the pneumococci, and not those which grow in clumps, such as the staphylococci. It seems probable that the mode of growth and chain formation of the former class favours extension along minute channels, vascular or otherwise, and this may be the explanation of the frequency with which this form of organism is associated with infective otitis media and its cerebral complications.

§ 2.—*Anatomical Considerations.*

The following communications of the tympanum, mastoid antrum and cells with surrounding structures are of importance :—

(1) The petrosquamous fissure, which runs along the whole length of the tegmen tympani, and which may remain patent for a varying number of years after birth.

(2) Mastosquamosal fissure which is marked by numerous foramina when ossified.

(3) Fossa subarcuata. This is a large opening in the cerebellar surface of the petrous bone, which in childhood transmits a process of dura mater containing a vein which terminates in cells beneath the superior semicircular canal. This process may persist as a strand of connective tissue, and a case has been reported [8], which will be mentioned later, where infection of the labyrinth took place by this path.

(4) Lateral and sigmoid sinus, by means of numerous minute veins.

(5) Superior petrosal sinus, by means of a small vein.

(6) Inferior petrosal sinus, by a vein from the labyrinth.

(7) Free communication through the bone with the duramatral system of veins.

(8) Jugular fossa, the root of which is pierced by a number of veins draining the floor of the tympanum.

The relations of the aqueductus Fallopii, which lodges the facial nerve, to the boundaries of the tympanic cavity may be considered at this point. The Fallopian aqueduct first comes into relation with the inner wall of the tympanum, where it lies above the fenestra ovalis; posteriorly to this point it curves downwards along the posterior wall. On the posterior tympanic wall is the pyramid which lodges the stapedius muscle, the tendon of which emerges from the apex of

this bony prominence to gain its point of attachment in the neck of the stapes. The cavity in the pyramid is prolonged into a minute canal which communicates with the aqueductus Fallopii, and transmits the tympanic branch of the facial nerve which supplies the stapedius muscle. Here, it will be seen, is a direct communication from the tympanic cavity to the interior of the aqueductus Fallopii, and this may possibly serve as a path by which infective micro-organisms may reach the sheath of the facial nerve. The bony walls of the canal are imperfectly ossified until some years after birth, and even when ossification has occurred congenital gaps in the bone are liable to persist. It is well known that children are relatively more liable to facial paralysis than adults during the course of an acute or chronic middle-ear suppuration; and this is explained by the fact that in these cases ossification is incomplete. Again, a special characteristic of tuberculous otitis media is the early destruction of bone, and facial paralysis is comparatively frequent in association with these tuberculous cases. Schwabach, indeed, considers that facial paralysis is eighteen times more frequent in tuberculous otitis media than in other forms.

Blood supply.—Arterial blood is brought to the internal ear by a branch of the basilar artery which enters the labyrinth along with the auditory nerve through the internal auditory meatus, while the middle ear is supplied chiefly by branches of the external carotid. Minute vessels perforate the bone at numerous points, and in many cases infection spreads by means of a septic thrombus originating in one of them. They run in the mucous membrane, and so are in close relation to pathogenic processes taking place in the interior of the ear. The veins empty into the lateral sinus and veins of the dura mater, and into a venous plexus round the Eustachian tube. In connexion with the blood supply of the labyrinth, some important communications with the tympanum and the surrounding structures are described by recent authorities on the subject.

(1) The blood-vessels of the tympanic mucosa send minute branches into the bony wall of the promontory.

(2) The blood-vessels of the dura mater penetrate an area between the semicircular canals at the fossa subarcuata.

(3) The blood-vessels of the temporal bone surrounding the labyrinth communicate with the vessels in its capsule.

Shambaugh [12], in a paper entitled "Relations in the Blood Supply of the Inner Ear," published the results of an investigation made by him as to the channel or channels by which venous blood

leaves the internal ear, and also as to whether communications exist between the blood-vessels of the tympanic mucosa and those of the membranous labyrinth and endosteum. In his paper he also gives the results arrived at by two different observers, Siebenmann and Eicher, in an investigation as to the first point, which are as follows:—

Siebenmann gives three channels by which venous blood leaves the internal ear, namely:—

(1) A vein in the internal meatus drained the blood from part of the cochlea.

(2) A vein along the aqueductus cochleæ drained the blood from the cochlea as well as the vestibule.

(3) A vein along the aqueductus vestibuli drained the semicircular canals and vestibule.

Eicher found only the second and third routes, while Shambaugh, in the pig, sheep, and calf found only the vein running along the aqueduct of the cochlea.

With regard to the second point, Shambaugh quotes Alexander on the communications between blood-vessels of the internal and middle ear, while he himself demonstrated that the branches of the labyrinthine artery, supplying the endosteum, penetrate the bony capsule at several points about the base of the cochlea and the vestibule, and that, apparently, in the ears of the calf at least, communications do exist between the blood-vessels of the tympanic mucosa and those of the membranous labyrinth and endosteum. If this is the case, it is possible that pathogenic organisms from the middle ear might infect the labyrinth through the medium of the blood-vessels.

§ 3.—*Pathological Considerations.*

As the result of infective disease in the middle ear, certain changes occur which give rise to alterations in the normal appearance of the various structures comprising the middle and internal ears. In the earlier stage of acute otitis media the vessels of the tympanic membrane become injected and reddened. Inflammatory exudation into the interior of the tympanum causes bulging of the tympanic membrane. Occasionally the membrane appears to be unusually resistant to ulceration and rupture; in these cases perforation is apt to be considerably delayed, and when it does occur may be so small that efficient drainage of the tympanic cavity is prevented. The mucous membrane lining the various cavities of the ear also undergoes certain changes. First of all, the mucosa becomes swollen, and exudes serum,

mucus, or blood; later on the inflammatory process extends to the deeper layers, and the exudation becomes purulent in character. When the disease becomes chronic, the superficial epithelium is lost, or exhibits metaplasia; the surface has a red and granular appearance. On this surface polypoid masses of exuberant granulation tissue may originate, and it is not uncommon to meet with these polypoid masses almost completely obliterating the lumen of the external auditory canal. The secondary tympanic membrane may also become involved in ulcerative processes, and may eventually be completely destroyed. As a result of these changes thickening, adhesions or scarring of the mucous membrane may occur.

The bony walls are also subject to the destructive action of the bacterial toxins, and in the course of chronic suppurative otitis media they first of all become thickened; later on, the infective process may lead to caries of the bone, in which condition its medulla is replaced by granulation tissue, more and more bone being destroyed until, eventually, perforation takes place, or necrosis, in which a small or large portion of the bone is completely cut off from its blood supply, with the result that death of that portion of the bone occurs, and a sequestrum is formed. These pathological processes are apt to affect the ossicles, and it is not uncommon to find them lying loose in the cavity of the tympanum.

The situations in which caries and necrosis appear to be most common are:—

(1) The mastoid region, most often in the outer wall or anterior wall.

(2) The roof or posterior wall of the mastoid antrum are often perforated or completely destroyed, with the result that infection of the meninges, lateral sinus or brain occurs.

(3) The inner tympanic and antral wall. Here small patches of caries may be present leading to labyrinthine fistulæ, thus opening up a path of infection into the labyrinth.

(4) The walls of the Fallopian aqueduct, which may be partially or completely destroyed, and the facial nerve left exposed.

§ 4.—*Intracranial Morbid Anatomy.*

This will be considered in the various sections which deal with the different intracranial lesions, but a few preliminary facts may be mentioned at this point in order to avoid repetition in the following pages.

The dura mater is composed of tough fibrous tissue which is, in

addition, often thickened by disease, and thus is enabled to offer a firm resistance to the passage of pathogenic micro-organisms through its substance.

In many cases of temporosphenoidal abscess perforation of the dura does occur, especially when the brain abscess is associated with an extradural collection of pus. It is not necessary, however, that perforation of the dura should precede infection of the pia and arachnoid membranes. MacEwan [9] considers the sequence of events which takes place in general meningeal infection, without perforation, to be as follows: When the bone is involved there is found on the visceral side of the dura a projection of granulation tissue, generally somewhat conical in shape, corresponding to the area of the bone affected. This gives rise to an indentation of the surface of the brain which causes the pia mater to become adherent to it. In this way the vessels of the pia mater may become directly infected from the primary focus in the ear without the dura mater being perforated. Owing to the pia mater being an exceedingly vascular structure, the infecting organism may be distributed by means of the vessels over a large area of the meninges, giving rise to a generalized suppurative leptomeningitis. Moreover, the pia mater gives off from its inner surface numerous minute vessels which extend perpendicularly downwards into the cerebral substance. This vascular arrangement, therefore, also favours extension of the morbid process to the interior of the brain.

When extension of the disease takes place into the lateral sulcus, the outer wall of the sinus becomes the seat of granulation tissue formation, which affords a natural protection against further infection of the sinus for the time being. Should the primary cause not be removed, either by natural arrest of the infective process or as a result of operative measures, sooner or later pathogenic organisms make their way through the sinus wall, giving rise to an endophlebitis. The inner wall becomes roughened and a deposit of fibrin takes place; this, by the deposition of successive layers, results in the formation of a thrombus, and the disease spreads along the sinus wall by continuity or by means of the anastomosing lymph spaces. Eventually the lumen of the vessel becomes blocked and a complete thrombosis is established.

In the case of infection of the sinus taking place from one of its small tributary veins, part of the clot within the latter projects into the lumen of the sinus and thrombosis in the latter takes place from this point.

If the primary disease be removed further infection of the thrombus

may be prevented, if not disorganization of the thrombus occurs, and it commences to break down and to form pus, which is then carried to various parts of the body, with, of course, the production of pyogenic abscesses. Should the inferior portion of the sinus be blocked by the thrombus it is possible for the thrombosis to extend backwards to the torcular Herophili, and so to the opposite lateral sinus.

Abscesses of the brain are usually met with in the white matter, and this is due to the fact that the cortex, owing to its vascularity, is capable of offering an effective resistance to the destructive powers of the bacterial toxins. Moreover, the piamatral vessels extend perpendicularly downwards into the grey substance where they terminate in minute capillaries. Infective emboli are carried to these terminal portions and form a nidus around which the destructive processes may extend.

Chapter I.—Lateral Sinus Thrombosis.

This complication was present in 55 of the total number of cases with infective disease of the middle ear, this being a percentage of 20·5.

Males were more liable to thrombosis of the lateral sinus than females, in the proportion of 33 of the former to 22 of the latter.

Lateral sinus thrombosis was of most frequent occurrence between the ages of 11 and 20, this decade contributing 21 cases, or 38 per cent. of the total number; while there were 13 cases, or 23·6 per cent. between the ages of 1 and 10. Only one case under the age of 1 year occurred, the youngest subject being aged 9 months. This case is of interest owing to the fact that it is uncommon for thrombosis of the lateral sinus to occur at such an early period of life. In no other decade did the cases exceed six in number. The oldest case noted was 60 years of age.

Lateral sinus thrombosis occurred in four out of the 31 cases of acute otitis media.

Some observers state that the right lateral sinus is more commonly affected than the left. In this series of cases this difference in favour of the right side was not appreciable, the right side being affected in 24, and the left in 23 instances. In six cases the disease was bilateral.

Analysis of Cases.

The majority of the 55 cases collected arose from spread of the disease into the sigmoid groove, and of these 18 were associated with extradural abscess.

Of the cases which belong to this class, 31 were produced by the disease involving the posterior tympanic wall or posterior wall of the antrum, or mastoid cells, and four through extension of the disease through the tegmen tympani.

In 13 there was either perforation or necrosis of the bony wall, infecting micro-organisms reaching the lateral sinus in this manner—while in 22 cases the bone was not affected. In 11 of the latter cases infection may have reached the sinus by direct contact of the latter with the bone separating it from the suppurating cavity, since these bony partitions are thin and it is quite possible for infection to take place in this way. It must be remembered, however, that these bony partitions are always perforated by small veins opening into the lateral sinus, and it is more than likely that in several of these cases infective phlebitis of one of the small veins was the origin of the sinus thrombosis.

Lateral sinus thrombosis is frequently associated with extradural abscess, but it is doubtful whether the latter can be considered to be the cause of the thrombosis in every case in which these two conditions are present together. The dura, as mentioned above, is a structure which is capable of prolonged resistance to the destructive action of bacteria and their toxins, and the micro-organisms have to penetrate two layers of the dura, namely, the endosteal and meningeal, before gaining access to the inner wall of the sinus. Moreover, it is not uncommon to find the dura covered by a layer of granulation tissue which forms one of the boundaries of a perisinus abscess, without symptoms of lateral sinus thrombosis being present. It is probable, therefore, that in some of these cases extension of the thrombotic process from a small venous tributary of the lateral sinus, and not the extradural abscess, was again responsible for thrombosis of the latter.

In eight cases out of the 55 the path of infection was through the small tributary veins of the lateral sinus. The proportion of cases originating in this way might seem to be a small one; it is a difficult matter, however, to demonstrate thrombosis of these small veins, and when we take into account the fact that thrombosis and infective phlebitis in them is bound to be of frequent occurrence in suppurative disease of the middle ear we must come to the conclusion that several cases included under the first heading more properly belong to the present class. Indeed, I think we may consider that the majority of cases of lateral sinus thrombosis originate in septic phlebitis and thrombosis of their small tributaries.

The two channels of infection, already mentioned, are responsible for most cases of sinus thrombosis.

Extension of the thrombotic process from a vein draining into the superior petrosal sinus, and from thence into the lateral sinus, was responsible for one case of the series. This path of infection appears to be comparatively rare. According to MacEwen, some of the labyrinthine veins drain into the inferior petrosal sinus, and therefore it might be possible for labyrinthine suppuration to be a cause of sinus thrombosis. No case of this kind occurred, and it would be difficult to demonstrate this path of infection, since suppuration in the middle-ear cavity in almost every case accompanies labyrinthine suppuration and the inferior petrosal sinus could, of course, be as readily infected from the former as from the latter.

Thrombosis in the jugular bulb and internal jugular vein, spreading upwards into the sigmoid sinus, occurred in one case. When the close relation of the jugular bulb to the floor of the tympanic cavity is considered, it might be expected that lateral sinus thrombosis due to this cause would be of comparatively frequent occurrence. These cases, however, appear to be rare; but if we bear in mind the fact that detection of a small thrombus in the jugular bulb is not an easy matter, even in a *post-mortem* examination, unless a special method is adopted, we must come to the conclusion that not a few cases are overlooked in which thrombosis in this situation has taken place. It is advisable, therefore, at the autopsy to examine the jugular bulb, not only in all cases of lateral sinus thrombosis, but also in those cases in which some form of general systemic infection has occurred without the lateral sinus being thrombosed. In order for the examination to be of any value it is necessary to resect that portion of the petrous bone which enters into the formation of the jugular fossa, special care being taken to remove a sufficiently wide area of bone, as well as the internal jugular vein. The walls of the vein and bulb can then be slit up and the lumen washed in a stream of water. In this way any roughening of their internal surfaces, indicating phlebitis, will be apparent.

In one case thrombosis spread from the lateral sinus of the opposite side, the thrombotic process extending backwards by the deposition of successive layers to reach the torcular Herophili and lateral sinus of the opposite side.

The question as to whether pyæmia can be caused by septic thrombosis of small veins in the bone, without the lateral sinus being affected, has been much discussed. In 24 cases of the present series, pyæmic, or

septicæmic processes took place in various parts of the body, without the lateral sinus being thrombosed, and there seems to be no valid reason why general septic infection should not occur from this cause. It is well known that acute infective osteomyelitis, of the tibia for example, may give rise to pyæmia through involvement of the smaller vessels, and therefore it is only reasonable to suppose that infective osteomyelitis of the petrous bone, with the accompanying thrombosis of its vessels, should be able to bring about a similar result. On the other hand, as already mentioned, it is very easy to overlook a small mural thrombus in the jugular bulb, which would be quite sufficient to give rise to a general systemic infection.

Cases have been reported [7] in which observers have made the most careful *post-mortem* examination and have come to the conclusion that general infection has occurred from osteomyelitis of the temporal bone with its accompanying venous thrombosis. It is not probable that in all the 24 cases noted in this paper this was the mode of infection, but I think that we may assume that some cases at least were due to minute venous thrombosis, and not to thrombosis of the lateral sinus.

In this connexion the subject of pyrexia in children, unaccompanied by physical signs pointing to a definite lesion in some particular part of the body, may not be out of place.

We may be at times considerably puzzled to account for rise of temperature in children in whom, though they are obviously ill, there are no definite signs upon which to base a diagnosis. I can recall several cases of this kind in the wards of St. Bartholomew's Hospital, in more than one of which meningitis was first suspected. In one or two cases disease of the ear was found to be the cause of the pyrexia, but in others no definite diagnosis could be arrived at, and in course of time the temperature fell to normal and the child rapidly improved in health. In some cases attention is directed to the ear by the child constantly raising its hand to the affected side, and in these cases tenderness on pressure being made, either over the mastoid process or directly inwards over the tragus, is elicited. In others there is nothing to direct attention to the ear as being the source of the trouble. I would suggest that in a good many of these cases of pyrexia of doubtful origin in infants the cause lies in the middle ear. Micro-organisms of an infective nature reach the tympanic cavity viâ the Eustachian tube. Suppuration may or may not occur; in the former case perforation of the drum will probably occur, in which event the pus escapes by the external auditory

meatus and the diagnosis becomes obvious; in the latter the infective process may extend to the numerous small veins which lie in the mucous membrane, and thus an absorption of the septic material into the systemic circulation takes place with its accompanying rise of temperature. It is probable that some cases of septic broncho-pneumonia arise in this way. Jacobi [6], in a paper on "Otitis Media in Children," discusses the question of septic absorption. His view is that in the young the lymphatic vessels are very active, and especially so in emaciated and atrophic subjects. In the presence of ear disease the epithelium lining the drum membrane and interior of the tympanum is often destroyed, thus permitting of more rapid absorption. These facts would explain the readiness with which absorption may take place from the interior of the ear into the lymph and blood circulation and lead to deposit in distant organs, with mild or serious sepsis or persistent elevation of temperature without obvious cause.

The paths of infection in the 55 cases of lateral sinus thrombosis are set out in the following table:—

I. Disease spreading into the sulcus lateralis			35 cases
(*a*) With extradural abscess	supra-tegminal	4	,,
	perisinus	14	,,
(*b*) Without extradural abscess—through posterior surface of petrous bone, mastoid cells or antrum	? by direct contact	11	,,
	with perforation of bone	6	,,
II. Thrombosis of small veins extending into the lateral sinus		9	,,
III. Thrombosis in internal jugular vein or bulb spreading upwards		1	,,
IV. Extension of thrombosis from sinus of opposite side		1	,,

There were nine cases in which the path of infection was doubtful. These are not included in the above list. It will be seen that the first class of case appears to be by far the most frequent, but, as has already been pointed out, a good many of the cases in this class might be more properly grouped under the second division.

In connexion, therefore, with this form of intracranial affection, I should wish to direct attention to the following points:—

First, the probability that, owing to their anatomical arrangement, the small venous tributaries of the lateral sinus are the most important factors in the production of lateral sinus thrombosis, and that thrombosis in them is responsible for the majority of cases.

Secondly, that with regard to the frequent association of extradural abscess with thrombosis of the lateral sinus, it is doubtful if the presence of an extradural (perisinus) collection of pus is always an indication

that thrombosis has occurred from extension of the micro-organisms contained in the former into the wall of the latter. In the majority of cases, no doubt, this has taken place, but there remain a few in which the thrombosis has an origin independent of the extradural abscess.

And thirdly, that general sytemic infection can and does occur, without thrombosis of the lateral sinus, from an infective osteomyelitis of the temporal bone.

Chapter II.—Brain Abscess.

Ear disease is responsible for about 35 per cent. of all cases of brain abscess; some observers, indeed, consider the proportion to be as high as 50 per cent.

Opinions differ as to whether temporo-sphenoidal abscess is more frequent than the cerebellar variety. Körner considers that the former is more common than the latter in the proportion of 63 per cent. to 31 per cent. Ballance, on the other hand, holds the opinion that cerebellar abscess occurs more frequently.

In this series of 42 cases of brain abscess, there were 30 of the temporo-sphenoidal to 12 of the cerebellar variety, or 71·4 per cent. of the former to 28·6 per cent. of the latter.

Taking both classes together the numbers appear to show that males are more liable to abscess of the brain of otitic origin than females, there being 28 cases in the male sex to 14 in the female.

In the present series of cases cerebral abscess was most common between the ages of 11 to 30, for 17 out of the 30 cases occurred in this period of life. The youngest subject was aged 6 months and was the only case under the age of 1 year. The oldest case noted was aged 45.

Out of the 12 cases of cerebellar abscess collected 8 were between the ages of 3½ and 30. No case occurred under the age of 3½, and the oldest case was in a subject aged 63. The cases of cerebellar abscess, however, are too few in number for much importance to be attached to these figures. It is, of course, most common to find temporosphenoidal and cerebellar abscesses as a result of infective middle-ear disease, but in a few cases the abscess may be situated in other parts of the brain. In these cases the infecting organism is carried by the blood-stream and the abscess is either the result of a general systemic infection, and is of a pyæmic nature, or of a simple transference from the primary disease in the ear by the local blood-vessels.

The other parts of the brain in which abscesses occurred were: the frontal lobe in three cases, the occipital lobe in two, and the parietal lobe in one case. With the exception of the two cases of occipital abscess, they were associated with either a temporosphenoidal or a cerebellar abscess and have not been included in the list of 42 cases of brain abscess.

The abscess may be acute or chronic, the latter variety being the more common. In the acute form the pathogenic organism is either of an especially virulent nature or the patient's powers of resistance are not so effective as they should be. If the lesion be chronic the surrounding brain matter is protected by the formation of a pyogenic membrane which limits the action of the toxic material. It is possible for a chronic abscess, thus encapsuled, to be present in the brain for a considerable length of time without causing any symptoms which might point to its existence. Usually, however, secondary infection of the abscess takes place, and if the organism responsible for it is of a virulent nature the chronic process may be transformed into an acute one, and the protecting capsule destroyed.

In the acute variety the walls are usually ragged and friable, while in the chronic form the walls are smooth and thick.

As far as can be ascertained from the *post-mortem* records, ten cases, including those of the pyæmic variety, were definitely acute, while six cases had thick abscess walls and were evidently chronic. In the remaining cases it was not possible to come to a definite conclusion as to whether the abscess was acute or chronic, though the majority of cases were most probably of a chronic nature. The contents usually consisted of greenish offensive pus; in one case of a tuberculous nature the contents consisted of caseous material, and one of the acute abscesses contained tarry, black, purulent material.

Condition of surrounding structures.—In cases of temporosphenoidal abscess the brain and its membranes were often adherent to the petrous bone, and in several cases a fistulous track led from the dura mater over the temporal bone into the abscess cavity. In other cases the pia mater and arachnoid were thickened and opaque and adherent to the brain. The brain matter in the neighbourhood of the abscess was often discoloured and softened, and in one case appeared to be undergoing a process of fatty degeneration.

Course and termination of an abscess.—The abscess may become chronic; if not, unless the collection of pus is drained by operation or drains itself through the external auditory meatus, it may burst into

the lateral ventricle with a rapidly fatal result to the patient, or into the subdural space, setting up a leptomeningitis which is also rapidly fatal, or it may cause death, owing to its large size or unfavourable situation, by pressure on the vital centres in the medulla.

§ 1.—*Cerebral Abscess.*

When this occurs as a result of infection from the middle ear, its situation is almost invariably in the temporosphenoidal lobe, owing to the close relation of the latter to the roof and posterior wall of the tympanum. Twenty-nine out of the thirty cases collected occurred in this lobe of the brain.

The following were the paths of infection in the thirty cases of cerebral abscess :—

(1) Infection through the tegmen tympani.

(2) Infection through the mastoid antrum, cells, or posterior tympanic wall.

(3) Infection through vascular channels.

(4) Formation of the abscess as a result of general systemic infection. The infective material is carried from the ear by the blood-stream, and conveyed by it to various parts of the body. Finally, it reaches the cerebral circulation, and is arrested in one of the minute arterioles, with the result that a pyæmic abscess is formed.

The first two channels of infection may be considered together. Of the thirty cases of cerebral abscess, infection through the tegmen tympani was responsible for twelve cases; while in five, extension of pathogenic micro-organisms took place through the posterior tympanic wall, mastoid cells, or antrum. In these two classes extradural abscess was present on seven occasions.

Condition of the bone.—Perforation took place in five cases, while in seven, although there was no actual perforation, necrosis of the bone was present.

Extradural abscess appears to be frequently associated with temporosphenoidal abscess of otitic origin. In most cases there is a track of caries through which pus has made its way, from the seat of the primary disease, to infect the meninges, with or without the formation of an extradural abscess. The dura mater, however, is a structure very resistant to the destructive action of pathogenic bacteria, and the probability is that an abscess will form. If this is not evacuated, either by natural means, in which case the pus makes its way through the diseased portion of bone with drainage through the

external auditory meatus, or by operation, sooner or later the pus will make its way through the dura to reach and infect the arachnoid and pia mater. It is not necessary, however, as has been pointed out, that there should be an extradural collection of pus, or that it should make its way through the dura for the interior of the brain to be affected with the formation of an abscess, for a localized pachymeningitis externa causes a bud of granulation tissue to project from the visceral surface of the dura. This projection gives rise to an indentation on the surface of the brain, causing the pia mater and arachnoid to adhere to the brain substance as well as the dura, with the result that infection can reach the latter through the vessels of the pia mater which send branches into the white matter.

Superficial abscesses in the cortex of the brain appear to be seldom met with, and this is probably due to the fact that the cortex, owing to its vascularity, is very resistant to the destructive action of bacterial toxins, and also to the fact that the blood-vessels afford an easier means of access into the white than the grey matter.

Condition of the dura mater.—In three cases it was thickened (pachymeningitis) and adherent to the brain, while in two cases it was covered with granulation tissue, and in a necrotic condition. It is probable that, in these cases, extension of the morbid process to the interior of the brain took place in the manner described above. In six of the seven cases associated with extradural abscess, the dura mater was perforated, and a fistulous track led from the abscess cavity into the interior of the brain. The dura mater was unaltered in one case.

Infection spread through the medium of vascular channels in four cases. Cases in which the cerebral substance external to the abscess cavity appears healthy in all probability originate in this way, but it must be remembered that the grey matter has great powers of recovery from the effects of disease, and it is possible that, in some cases where no fistulous track is evident, the line of communication with the exterior of the brain has been obliterated.

The veins which run in the mucous membrane lining the cavity of the middle ear drain partly into the veins of the dura mater, and an infective thrombus originating in one of the veins of the tympanic mucosa may reach one of the dural veins; the latter infects one of the piamatral system, and from this point the process can extend into the interior of the brain.

In some instances branches of the cerebral arteries which supply the temporal bone may become thrombosed, and minute infective

emboli carried into their terminal branches in the white matter, thus forming a nidus around which pathological processes extend, giving rise to a cerebral abscess.

The perivascular lymphatics also are sometimes responsible for a similar result, especially when the original disease in the ear is of a tuberculous nature.

The fourth group of cases is that in which the abscess is a result of general systemic infection, with the formation of metastatic deposits of infective material in the interior of the brain. These abscesses are said to occur most commonly in those parts of the brain which derive their blood supply from the sylvian artery of the left side, and also in those parts which are situated at the base. I have been unable to collect any cases either in support or disproof of this view.

In one case of the series the brain abscess was purely pyæmic in character, though in three other cases a pyæmic abscess was present in addition to one of direct otitic origin.

One of the remaining cases was most probably due to an exploratory puncture of the brain at a previous operation; in the other seven I could not come to any conclusion as to the path of infection, owing to insufficient details being given in the *post-mortem* records.

The following table gives the varieties and frequency of the different paths of infection in thirty cases of cerebral abscess:—

I.	Infection through mastoid cells, antrum or posterior tympanic wall	5
II.	,, ,, tegmen tympani	12
III.	,, ,, vascular channels	4
IV.	,, ,, exploratory puncture of the brain at a previous operation	1
V.	Pyæmic	1
	Doubtful cases, not classified	7

These figures show that the path of infection, in most cases of temporosphenoidal abscess of otitic origin, is through the roof of the tympanum. The most rational method of treatment, therefore, to adopt in a case of this kind is to perform the radical mastoid operation with exposure of both cranial fossæ. Thus, if the sigmoid sinus is healthy, the temporosphenoidal lobe should be punctured directly upwards through the dura covering the tegmen. This method offers a very much better chance of finding the intracranial abscess than the operation, performed by some surgeons, of trephining the bone over that portion of the brain where the abscess is supposed to lie.

The above are the more common channels of infection, but one which is of interest, though it rarely occurs, may be mentioned: namely, that in which infection is conveyed by one of the various processes of dura

mater which enter foramina in the temporal bone. Kümmel [8] reports a case in which this occurred. The process of dura mater concerned in this case was the one passing into the fossa subarcuata, to which attention has already been called. It was represented by a band of connective tissue extending from granulations in the mastoid, from which the infection originated, to the perforated area in the upper part of the petrous bone.

§ 2.—*Cerebellar Abscess.*

Twelve cases of this variety of abscess occurred and the paths of infection noted were :—

(1) Through the posterior tympanic wall, mastoid cells or antrum as a result of necrosis or perforation of the bone, with or without the formation of an extradural abscess.

(2) By infection spreading from the lateral sinus.

(3) By infection spreading from the labyrinth.

Group 1.—Four cases arose as a result of infection spreading in this manner, and of these, perforation or necrosis of the bone was present in three instances—and perisinus abscess also occurred in these three cases—while the fourth was the result of infection through the posterior tympanic wall without the formation of a perisinus abscess. This pathway of infection is similar to that which occurs in cerebral abscess and the same remarks therefore apply.

Group 2.—*Infection through the lateral sinus.*—Most cases of cerebellar abscess are in direct contact with the sigmoid sinus, and the way in which pathogenic organisms reach the cerebellum may be as follows : When the whole circumference of the sinus is involved and is the seat of infective organisms, the cerebellar veins may become infected and thrombosis result. By this means the bacteria which are responsible for the primary disease, or in some cases those which have brought about a secondary pyogenic infection, are conveyed to the interior of the cerebellum to form a nidus which is the starting point whence the bacterial toxins may commence their destructive processes. In other cases the dura mater may become thickened, in the way described under the section dealing with cerebral abscess, thus bringing the duramatral system of veins into communication with the veins of the pia mater.

Three cases were due to infection spreading from the lateral sinus, and in one of these the sinus was filled with greenish pus. Direct extension to the tentorium cerebelli took place, with the formation of a superficial abscess cavity in the cerebellum. This communicated by

a track the size of a pin's head with a second deeper abscess in the lateral lobe.

Group 3.—*Infection through the labyrinth* is an important source of cerebellar abscess. In four out of the twelve cases collected the spread of infection took place through the internal ear. In three of these cases it occurred in young subjects—their ages being $3\frac{1}{2}$, 4, and 19—while in the fourth case the age was not stated.

It is now recognized that infective disease of the labyrinth is responsible for many more cases of cerebellar abscess than was formerly thought to be the case, and that it is one of the more important, if not the most important, causes of abscess formation in the cerebellum. According to Okada a preponderating majority of cerebellar abscesses follows labyrinthine suppuration, and only a third are secondary to sinus disease. The subject of labyrinthine infection as a cause of encephalic suppuration will be more fully dealt with in the section dealing with meningeal affections of the brain; there the various points at which infection may gain entrance to the interior of the internal ear will be noted, as well as the paths whereby the infective organisms may leave it.

With regard to the actual manner in which infective micro-organisms reach the brain, in cases of cerebellar abscess due to infection from the labyrinth, the probable sequence of events is as follows: Pathogenic organisms leave the internal ear through the internal auditory meatus along the sheath of the eighth nerve. Infection of the meninges takes place, giving rise to a local pachymeningitis, and spreads from this point in the manner described above to the interior of the cerebellum.

It is possible for the cerebellum to be infected through the veins in the tympanic mucosa, in a similar manner to that described under cerebral abscess. No case of this kind occurred in the collected cases of cerebellar abscess.

Spratt [14] has described a case in which leptomeningitis occurred as a result of infection of the meninges by means of the sheath of the facial nerve. It would seem possible, therefore, that supposing in this case the infecting organisms had not been sufficiently virulent to produce a generalized leptomeningitis, or that the resisting power of the dura mater had been greater, local pachymeningitis might have resulted; in which case infection of the cerebellum, with the formation of an abscess in its substance, might have taken place. One would expect that, if this is a possible path of infection, children would be more liable to cerebellar abscess, for in early life the canal in which

the facial nerve lies is imperfectly ossified, and it is well known that facial paralysis, resulting from infective disease of the middle ear, is relatively more common in children than in adults.

In tuberculous disease of the middle ear destruction of the bone is often early and very extensive, and facial paralysis is often an early symptom. One would expect, therefore, in these cases also, that, as infection of the facial nerve sheath is frequent, cerebellar abscess might result in a good number of cases. I have not been able to discover any case in which cerebellar abscess was caused in this way.

We may conclude, therefore, that although this path of infection may be possible, it is of very rare occurrence.

Another case was reported [13] in the *Archives of Otology* in which a cerebellar abscess was situated in the base of the cerebellum. Pus had tracked between the two tables of the temporal bone from the mastoid antrum and had thus infected the cerebellum. This is another rare pathway of infection in cerebellar abscess and need not be further considered.

TABLE OF PATHS OF INFECTION IN TWELVE CASES OF CEREBELLAR ABSCESS.

Mode of infection	Cases
Through posterior tympanic wall, mastoid cells or antrum	4
,, lateral sinus	3
,, labyrinth	4
Paths doubtful	1

No cases occurred in which the cerebellar abscess was due to infection through the vessels of the tympanic mucosa, or as general systemic infection with the formation of a metastatic abscess. These modes of infection, however, are of importance and probably occur almost as often as they do in cases of cerebral abscess.

CHAPTER III.—MENINGITIS AND EXTRA- AND INTRA-DURAL ABSCESS.

§ 1.—*Pachymeningitis.*

This term is applied to inflammation of the dura mater, and the inflammatory process may be simple or purulent. It most commonly affects the outer surface of the dura, in which case the condition is known as pachymeningitis externa. The internal or visceral layer may be affected as a result of the inflammation spreading through the meshes of the external layer, or in a few cases as a result of suppurative inflammation of the pia-arachnoid; the condition is then termed pachy-

meningitis interna. The inflammatory process may remain of a simple nature, but, if the primary cause be not removed, either by natural arrest of the ear disease or by operation, the simple inflammation may be transformed into a purulent one. If the pus formation continues the dura mater will be stripped from the bone to make room for the collection of pus, and an extradural abscess results.

I have collected twenty-five cases of otitic pachymeningitis exclusive of extradural abscess, in which the condition of the dura was noted. It is probable, however, that inflammatory changes of a slighter degree were present in many of the remaining cases. These, together with thirty-four cases of extradural abscess, illustrate the different degrees of pachymeningitis which may occur, varying from a simple infection of the dura to an extensive extradural abscess containing an ounce of pus.

The cases of pachymeningitis may be classified according to their pathological nature, as follows:—

(*A*) *Simple* (*non-purulent*).—The earlier stage of pachymeningitis observed was slight injection of the dura mater; in the next stage the inflammation was more marked, the dura being distinctly reddened and having a granular appearance, sometimes also being coated with lymph.

(*B*) *Adhesive.*—In this form there is the formation of a plastic exudate which binds the dura mater to the bone, pia-arachnoid, or to both bone and pia-arachnoid.

(*C*) *Purulent.*—In the early stage the dura is covered by a layer of granulation tissue from which exudes purulent lymph or actual pus. At a later stage of the purulent process pus collects between the dura and the bone, stripping off the latter from the former and giving rise to an extradural abscess.

(*D*) *Necrotic.*—In this form the proper blood supply of the dura mater is interfered with, or the infective organisms are especially virulent and the membrane becomes grey and sloughy, leading to—

(*E*) *The perforative form.*—The necrotic portion gives way and a perforation of varying size results.

(*F*) *Tuberculous.*—The most common variety observed was the adhesive form. The dura was adherent to the pia-arachnoid and brain in six cases, to the bone in two, and to both brain and bone in two cases.

A local pachymeningitis, by causing adhesions between the dura and pia-arachnoid, tends to prevent the spread of infective micro-organisms to the brain; should ulceration of the adherent membranes, however,

take place, or should the simple process be transformed into a purulent one, infective phlebitis in the veins of the pia mater is likely to occur and a generalized leptomeningitis or brain abscess results.

The perforative form may set up a leptomeningitis, pathogenic organisms making their way into the intradural space.

Purulent pachymeningitis usually gives rise to an extradural abscess. Pachymeningitis also frequently accompanies lateral sinus thrombosis, and, in some cases, is responsible for the thrombosis.

Tuberculous pachymeningitis.—Two cases of this variety occurred. In one of them the dura was inflamed and its visceral surface covered with pus, infection having taken place through the petrous bone, which was extensively diseased ; in the other there was coarse tuberculosis of the dura in the posterior fossa of the skull infiltrating the occipital lobe of the brain.

Condition of the bone.—The bone beneath the affected portion of the dura was often discoloured, sometimes even black. In some cases it was reddened and rough, in others it was carious and necrotic and its dural surface covered with granulation tissue. In other cases again there was perforation leading into the tympanum, mastoid antrum, or cells. Finally, the bone may be unaltered, in which case the dura mater has become infected, most probably as a result of the infective phlebitis of one of the veins of the tympanic mucosa extending into a vein of the dura mater.

§ 2.—*Extradural Abscess.*

This may be the result either of a purulent pachymeningitis, or of perforation of bone, in which case pus makes its way through the perforation to form an abscess beneath the dura mater, between it and the bone. This form of abscess was present in 34 out of the 267 fatal cases with infective ear-disease, and the positions in which the pus was situated were : Nineteen cases in the neighbourhood of the sulcus lateralis (12 of which were perisinus abscesses), 14 cases over the roof of the tympanum (suprategminal abscess) and 1 case at the apex of the petrous bone.

Abscess in neighbourhood of lateral sulcus.—The neighbourhood of the sulcus lateralis is the most common situation in which to find an extradural abscess, and infection appears to spread through the posterior tympanic wall in the great majority of cases. Thirteen cases arose in this way, five originated from the mastoid antrum or cells, while in one case infection appeared to have spread from the labyrinth

viâ the aqueductus vestibuli, and gave rise to an empyema of the saccus endolymphaticus. Many of these cases were associated with thrombosis of the lateral sinus and in one case the sinus wall was perforated. In this case it is probable that the lateral sinus thrombosis was the cause of the perisinus abscess. It is possible for a collection of pus within the sinus to be present together with a perisinus abscess and yet for the two to be independent of one another. In a case such as this the wall of the sinus will be deprived of its proper blood supply and will probably perforate, and the extra- and intra-venous collection of pus become a single abscess; so that when a collection of pus is discovered *post-mortem* within and around the sinus it is not always possible to tell whether the former is responsible for the latter or *vice versa*, or whether both arose from independent sources.

This form of extradural abscess may:—

(1) Discharge externally by perforation of the mastoid process, or through the foramen for the emissary vein, or through the mastoid antrum, or cells, and so through the external auditory meatus.

(2) Involve the lateral sinus.

(3) Set up a leptomeningitis in the posterior fossa.

(4) Give rise to a cerebellar abscess.

(5) Cause tempero-sphenoidal abscess by spreading upwards and anteriorly over the posterior edge of the petrous bone.

§ 3.—*Suprategminal Abscess.*

The roof of the tympanum as a site for an extradural abscess comes next in order of frequency. Suprategminal collections of pus are commonly associated with an abscess of the temporosphenoidal lobe of the brain, the latter often being adherent to the dura mater, forming the inner wall of the extradural abscess. It is common to find a perforation of the wall leading into a fistulous track communicating with the cerebral abscess cavity.

The pus may spread in the following directions:—

(1) Upwards, giving rise to a temporo-sphenoidal abscess.

(2) Backwards, over the posterior margin of the pars petrosa, forming a perisinus, in addition to a supra-tegminal, abscess.

(3) Outwards, along the superior surface of the petrous bone. It may terminate by perforating the tegmen tympani and draining into the tympanic cavity, or by bursting through the dura mater into the intradural space, setting up a diffuse leptomeningitis.

In one case the abscess was situated at the apex of the pars petrosa

and was most probably of vascular origin. An extradural abscess may be situated around the carotid artery in the carotid canal. This situation, however, is a rare one, and no abscess of this kind occurred as a complication in any of the cases collected.

Condition of the bone.—In nine cases the bone was carious and necrotic, although not actually perforated; in five cases it was perforated, and in four cases it was unaltered. In the remaining sixteen cases no note was made as to the state of the bone. In the four cases in which the bone was unaffected and probably in several of the others, in which no note was made as to its condition, the pathway of infection was in all probability a vascular one, as in the case of pachymeningitis without abscess formation. These cases in which the bone is not carious or necrotic are of interest clinically, since they are often accompanied by frequent and severe rigors with high temperature, although there is no evidence that the lateral sinus is thrombosed. In these cases complete recovery may take place after drainage of the abscess without any exploration of the sinus or ligature of the internal jugular vein. On the other hand, in those cases of perisinus abscess in which the bony partition between the dura and the middle ear has been extensively destroyed the symptoms are often of a comparatively mild nature.

Condition of the dura mater forming the abscess wall.—The dura may be stripped from the bone over a considerable area, its endosteal surface may be reddened and covered with granulation tissue and fibrinous deposits if the abscess is acute; if of a more chronic nature it may have the appearance of a pyogenic membrane. In the later stages of the disease, or if a secondary infection occurs, the walls of the abscess may become sloughy and necrotic, and finally perforate; the perforation in these cases varying from the size of a pin's head to that of a sixpenny-piece. The size of the abscess varied from a minute one not much larger than a small pea, to one of considerable size containing an ounce of pus.

Pachymeningitis may be simple or purulent. If the former is of the adhesive variety the dura mater may become gummed to the bone and pia-arachnoid, and so to the brain by a plastic exudation. This matting together of the membranes forms a barrier which tends to prevent the passage of pathogenic organisms through it. Should the simple pachymeningitis, however, be converted into a purulent one this matting together of the dura- and pia-arachnoid affords a pathway of infection to the vessels of the pia mater directly from the ear.

There are two main pathways of infection, namely, through the bone or through some vascular channel, such as the small veins of the dura mater or the lateral sinus, but it is probable that infection spreading from the lateral sinus is a comparatively uncommon cause of pachymeningitis, since the veins of the tympanic mucosa are likely to be involved in many more cases than is the lateral sinus.

§ 4.—*Intradural Abscess.*

A localized collection of pus in the intradural space is known as an intradural abscess. I have only been able to find three cases of this form of abscess, two of which were situated in the posterior fossa of the skull, and the other in the middle fossa. In the first case, the abscess was lying in the meshes of the pia mater, over the base of the occipital lobe of the brain; in the second case, it was placed over the roof of the tympanum, and the bone in this position was carious and necrotic. The third case was due to a necrosis of the labyrinth and was situated on the under-surface of the cerebellum.

An abscess of this kind is usually secondary to an extradural collection of pus which has escaped through a perforation in the dura mater into a part of the intradural space which has been shut off from the general cavity by adhesions. The abscess may, however, be formed without any preceding extradural abscess, and such cases must have a vascular origin.

§ 5.—*Serous Meningitis.*

I have included under this heading those cases of infective otitis media which are accompanied by an increase in the normal amount of either the subarachnoid or ventricular fluid, or of both together. In thirty-six cases a definite increase in the subarachnoid or ventricular fluid was present, and in several of them the ventricles were greatly distended with a large excess of cerebrospinal fluid. The fluid was either quite clear or was slightly turbid. The cases have been classified according as to whether the excess of fluid was in the subarachnoid space or the ventricles, or both together, thus:—

(1) Meningitis serosa externa ... ... 8 cases.

The excess of fluid is confined to the subarachnoid space.

(2) Meningitis serosa interna ... ... 21 cases

In this variety the ventricles of the brain are alone affected. This condition is also known as internal hydrocephalus.

(3) Meningitis serosa externa et interna ... 7 cases.

In this variety there is excess of fluid in both ventricles and subarachnoid space.

It will be noticed that most cases appeared to be of the ventricular variety, but it is possible that some of these were also accompanied by an effusion into the subarachnoid space, and that the latter collection of fluid escaped during the process of extracting the brain from the skull, and so was overlooked.

Twenty-three of the cases were associated with a leptomeningitis, which was either chiefly or entirely limited to the base of the brain, and seven occurred in conjunction with a more generalized meningitis. Of the remaining six cases, two were associated with cerebellar abscess alone, and there was no evidence in these cases that the abscess was leaking—one with intradural abscess and lateral sinus thrombosis, one with perisinus and cerebellar abscesses; while the last occurred in a case of general tuberculosis without any intracranial complication being present. With regard to those cases which were associated with leptomeningitis—perisinus abscess was present as an additional complication in four cases, labyrinthitis in five, temporosphenoidal abscess in one, and a suprategminal extradural abscess in one case.

An increase in the normal amount of cerebrospinal fluid may occur in the course of infective disease of the middle ear, especially in the chronic variety; but it is stated to be more frequently present when labyrinthitis or perisinus abscess occurs as a complication (Barr). The effusion may be acute or chronic, and in some cases the serous fluid may collect so quickly as to produce pressure on the cerebral blood-vessels, ending in their occlusion, and the rapid death of the patient (meningitis serosa maligna). Occasionally the fluid may be limited by adhesions. In one case a localized leptomeningitis in the neighbourhood of the internal auditory meatus formed a cyst-like collection of fluid surrounding the intracranial portions of the seventh and eighth nerves.

Causation.—The pia mater is a vascular membrane, consisting of a minute plexus of blood-vessels held together by extremely fine areolar tissue. It invests the entire surface of the brain, dips down between the convolutions, and forms at the base of the brain the velum interpositum and choroid plexuses of the ventricles. These are formed by an ingrowth of the pia mater, and in the lateral ventricles they consist of the vascular-fringed borders of the velum interpositum. They communicate with each other at the foramen of Monro, and are prolonged backwards as far as the choroid plexuses of the third ventricle. Those of the fourth

ventricle are formed by a similar process of pia mater, the tela choroidea inferior.

Owing to this arrangement of the pia-mater, inflammation, especially of its basal portion, can easily extend to the vessels of the choroid plexuses, and lead to an increased exudation of fluid into the ventricular cavities. Direct or indirect communications exist between the ventricles, and if these are not obliterated by adhesions, the fluid may spread to the other ventricles, and cause a general distension of the ventricular system.

In thirty out of the thirty-six cases a definite leptomeningitis, either simple or purulent, was present, and in twenty-three of the cases it was either confined entirely to the base, or else the base was more gravely affected than other parts of the brain. In the remaining six cases, five were associated with either extradural abscess, brain abscess, or lateral sinus thrombosis, and it is extremely likely that in these cases also there was a localized inflammation of the pia mater.

It is probable, therefore, that most cases of serous meningitis and internal hydrocephalus are caused by an inflammation of the pia mater, especially if the inflammatory process is situated at the base of the brain.

In those cases in which the labyrinth is involved, inflammation may spread along the sheaths of the seventh and eighth nerves, and so reach the pia mater which forms the tela choroidea inferior, leading to a dilatation of the vessels of the choroid plexus in the fourth ventricle, and an increased output of fluid into that cavity; or possibly along the aqueduct of the vestibule into the intradural space, giving rise to an increased production of subarachnoid fluid.

Some cases, no doubt, are unassociated with any gross inflammatory changes in the serous membranes of the brain, and in such cases toxins produced in the ear and circulating in the blood may stimulate the membranes to hypersecretion. It has been suggested that the severe cerebral symptoms, such as headache and vomiting with pyrexia, which are occasionally observed during the course of a chronic middle-ear suppuration in children and young adults, may be due to mild attacks of serous meningitis.

There remain a few cases associated with infective ear disease, in which serous meningitis and œdema of the brain and its membranes may be due to lesions in other parts of the body, and not directly to the ear disease. It is well known that this condition sometimes occurs in extreme venous dilatation from obstruction, as in mitral stenosis; in Bright's disease also a similar condition is occasionally present.

We may conclude, therefore, that while in the great majority of cases serous meningitis and internal hydrocephalus are due to an inflammation of the pia mater, yet there are some cases in which there is no obvious lesion of that membrane. Cases such as these may be due to toxins circulating in the blood, and that a third group of cases may exist in which, although infective disease of the middle ear is present, the serous effusion is due to some other cause, such as venous obstruction or general toxæmia.

§ 6.—*Purulent Ventricular Meningitis.*

A collection of purulent fluid was found in the ventricles of the brain in fifteen cases. Of these, six were due to the rupture of a cerebral abscess into the ventricle. Of the remaining nine cases, five were associated with leptomeningitis alone, and four with leptomeningitis and some other intracranial complication, namely, temporosphenoidal abscess in two cases, and labyrinthitis and perisinus abscess in one case each.

A purulent inflammation of the pia-arachnoid membrane is probably responsible for those cases of purulent ventricular meningitis which are not due to the rupture of a cerebral abscess into the ventricle, and the mode of infection is probably similar to that which occurs in simple ventricular meningitis.

§ 7.—*Tuberculous Meningitis associated with Infective Otitis Media.*

I have collected all the cases of tuberculous meningitis upon which *post-mortem* examinations have been made at St. Bartholomew's Hospital during the last fourteen years, with the object of ascertaining, first, the proportion of tuberculous meningitis cases associated with tuberculous or other infective disease of the ear, and, secondly, whether the ear can be considered as the primary focus of infection in any considerable number of cases.

The total number of tuberculous meningitis cases upon which autopsies were held was 368, and of these thirty were associated with infective disease of the ear, this being a percentage of 8·1. Bilateral otorrhea was present in fifteen cases, so that the total number of ears affected was forty-five. It is probable that infective ear disease was present in other cases also, since in a good many instances the ears were not examined. In only one case of tuberculous meningitis was a histological examination of the labyrinth made, and this revealed bilateral labyrinthitis, secondary to the meningitis. It is also possible that, in some of the cases with bilateral disease of the ear associated

with tuberculous meningitis, if the labyrinth had been examined it would have been found to be diseased.

In twenty-one of the thirty cases there was a definite focus of dissemination in other parts of the body, such as a breaking-down caseous lymphatic gland. There remain nine cases in which no focus, other than the ear was discovered.

In the series of 267 cases of infective otitis media, eight were of a tuberculous nature, and in the majority of them the destruction of bone was considerable. In five of them tuberculous meningitis occurred as a complication, and in four of the latter cases no obvious focus could be found in other parts of the body.

The cerebral blood-vessels are accompanied by perivascular lymphatics, while the pia mater itself is very rich in lymphatic vessels, and is therefore a particularly favourable structure for deposits of tuberculous material. Moreover, the stylomastoid artery, which is the main vessel of supply to the tympanic mucosa, anastomoses with the internal auditory artery which ramifies in the pia mater at the base of the brain. This anatomical arrangement, therefore, favours the spread of tubercle bacilli from the tympanum to the pia mater.

Three cases occurred in which infection by spreading along the lymphatics caused tuberculous intracranial lesions. In one of them there was coarse tubercle of the dura in the posterior fossa, in the second a tuberculous temporosphenoidal abscess resulted, and in the third there was a tuberculous tumour in the cerebellar peduncle. Each of these cases was accompanied by tuberculous meningitis, and it is very probable that the meningitis was caused in a similar manner by infection spreading along the perivascular lymphatics.

Fifty-five per cent. of the cases of tuberculous meningitis occurred between the ages of 1 and 5, and it is known that tuberculous otitis media is especially common in children. It is possible, therefore, that the preference of tubercle for the base of the brain may be explained, in some cases, by the fact that infection has taken place through the ear.

Another possible, though perhaps rarer, channel of tuberculous infection is through the labyrinth, for tuberculous disease of the middle ear is frequently associated with destruction of the outer wall of the labyrinth, especially the promontory. In one case the whole of the middle and inner ear was destroyed.

Hertzog (Munich) examined after death the ears of 100 males who were the subjects of pulmonary tuberculosis, and found that seventeen

had chronic suppurative otitis media (twenty-one ears in all). Five per cent. of these had labyrinthine suppuration. Kümmel (Hamburg) also considers that labyrinthine suppuration is especially frequent in tuberculous otitis media, for in twenty-six cases operated on by him tuberculous disease of the internal ear was present in six cases. [4].

The evidence that I have been able to collect is not sufficient for any definite conclusion to be drawn, but the frequency with which tuberculous meningitis is associated with infective otitis media suggests the possibility that tuberculous otitis may be a more frequent source of meningeal infection than it was formerly thought to be. It is also possible that general tuberculosis, in some cases, may have its infective source in the middle ear. In the great majority of cases, however, it is probable that the meningitis arises from an independent focus, such as a breaking-down caseous lymphatic gland. In order to properly investigate this subject it is necessary that histological examination of the petrous bone should be made in a large number of cases of tuberculous meningitis.

Chapter IV.—Leptomeningitis.

Ninety-eight cases of infective leptomeningitis associated with infective disease of the ear, excluding those of a tuberculous nature, have been collected. The paths of infection are indicated in the following table :—

I. *Secondary to*—	
(*a*) Cerebral abscess	9 cases
(*b*) Disease of lateral sinus	11 ,,
(*c*) Extradural abscess	12 ,,
(*d*) Cerebellar abscess	2 ,,
II. *Due to direct spread of the disease from*—	
(*a*) Tegmen tympani, mastoid cells or antrum	6 ,,
(*b*) Labyrinth	12 ,,
III. Secondary to pneumonia	6 ,,
IV. Due to exploratory puncture of brain	1 ,,

In thirty-nine cases the path of infection was uncertain.

The situations in which the meningitis was present were :—

Base of the brain	54 cases	Basal only	40 cases
		Cerebrospinal	14 ,,
Generalized	36 ,,		
Lateral hemisphere alone	5 ,,		
Ventricle	2 ,,		
Frontal	1 ,,		

§ 1.—*Leptomeningitis Secondary to Cerebral Abscess.*

One of these cases was due to an abscess in the frontal lobe, the remainder were secondary to temporosphenoidal abscess. The meningitis was confined to the base of the brain in six cases, to the left cerebral hemisphere and basal region in two cases, and was generalized in one case. The inflammation was non-purulent in two instances.

Causation.—If the abscess is separated from the surface of the brain by a small portion of grey matter, the pia mater may be infected by direct contact. Should the abscess be situated at a deeper level it may cause meningitis in the following way: The blood-vessels of the pia mater dip down into the white matter, which is often softened and infected in the neighbourhood of the abscess, especially if the latter is of the acute variety, or has become secondarily infected; an infective endophlebitis results and pathogenic organisms are conveyed by the blood-vessels to the pia mater, giving rise to a localized or diffuse meningitis, according as to whether the pathological process is limited by adhesions or not. Finally, the abscess may burst into the intradural space and set up a meningitis which is apt to be very acute and rapidly fatal.

§ 2.—*Leptomeningitis Secondary to Lateral Sinus Thrombosis.*

In six out of the eleven cases of meningitis secondary to this lesion the thrombus was septic, and in three of these cases it was purulent. In the other five cases no mention was made of the nature of the clot. The inflammation of the meninges was limited to the base of the brain in six of the cases, and to the left lateral hemisphere in one case, while in four cases the distribution was general.

Lateral sinus thrombosis can set up a leptomeningitis in the following ways:—

(*a*) By direct contact.

(*b*) By extension of the septic process along one or more of its venous tributaries, i.e., the inferior cerebral and cerebellar veins.

(*c*) By perforation of the inner wall of the sinus taking place with escape of the contents into the intradural space.

§ 3.—*Leptomeningitis Secondary to Extradural Abscess.*

Of the twelve cases in which leptomeningitis was secondary to extradural abscess, seven were due to perisinus abscess, three to suprategminal abscess, while one case resulted from an abscess at the

apex of the petrous bone and one from an empyema of the saccus endolymphaticus. With regard to the latter case, it should be mentioned that as no histological examination of the petrous bone was made, this case has been included under this heading and not among those cases secondary to infective labyrinthitis. Passow (Berlin) reports a case in which macroscopically a typical empyema of the saccus endolymphaticus was made out; microscopically, however, the aqueductus vestibuli and saccus were found to be unaffected and that an extradural abscess had simulated an empyema of the sac. Without a histological examination of the petrous bone, therefore, it is impossible to say whether an empyema was present in this case or not.

The meningitis was basal in ten cases, and confined to the right or left lateral hemisphere of the brain in the other two cases.

Causation.—The dura was perforated in seven cases and the pus had escaped into the intradural space, thus infecting the leptomeninges. In the remaining cases infection of the pia-arachnoid was brought about by direct contact, or possibly through venous infection.

§ 4.—*Leptomeningitis Secondary to Cerebellar Abscess.*

Of the two cases of meningitis secondary to an abscess of the cerebellum, the first was non-purulent, the pia-arachnoid covering the abscess being thickened and opaque; in the second the surface of the arachnoid over the upper and outer surface of the cerebellum was coated with yellow lymph. The pia-arachnoid was probably infected by direct extension from the abscess, since the latter in both cases was very near the surface of the brain and separated from the pia mater by only a very thin layer of brain substance.

§ 5.—*By Direct Extension from the Tegmen Tympani, Mastoid Cells or Antrum.*

In six cases the pia-arachnoid may have been infected by direct extension of the disease from the middle ear or its accessory cavities. In four of the cases the bone was carious, and it is possible that the organisms concerned may have directly infected the dura, which in turn infected the vessels of the pia-arachnoid. It seems more probable, however, that the meningitis was caused by an infective thrombosis of a vessel of the tympanic mucosa, continuous with a meningeal vein. This also was probably the path of infection in the two cases which were unassociated with bone disease.

§ 6.—*Infection of the Leptomeninges from the Labyrinth.*

Infective disease of the labyrinth is one of the most important causes of meningitis of otitic origin. Heine [3] reports that fatal otitic meningitis was caused by the labyrinth in 42 per cent. of his cases, while the percentage in Whitehead's series of cases was 27.

Although infective labyrinthitis only gave rise to meningeal infection in twelve of the present series of cases, or 12.2 per cent., it is probable that this percentage is too low, since histological examinations of the petrous bone were only made in the later cases, and without microscopical evidence we cannot exclude the possibility of the labyrinth being the path of infection. In several of the thirty-nine cases, in which the path of infection was uncertain, it is extremely probable that the labyrinth was responsible for the meningitis.

In this section the pathology of labyrinthitis will first be considered, secondly the channels of infection from the middle to the internal ear, and thirdly the paths along which pathogenic micro-organisms are enabled to travel from the labyrinth to the meninges.

Pathology of infective labyrinthitis.—Infective labyrinthitis may be either of the acute or chronic variety. In the acute form the disease is usually diffuse, but is sometimes localized to one portion of the labyrinth. Macroscopically the membranous labyrinth is injected and inflamed, and instead of presenting its normal whitish appearance is bright red in colour. Its cavities may be filled with blood-stained fluid, which later may become purulent; or there may be pus in one chamber and hæmorrhagic effusion in another. Thus in one of the cases [10] the vestibule contained purulent fluid, from which a pure culture of streptococci was grown. The semicircular canals contained hæmorrhagic effusion, while the cochlea contained purulent fluid in its lower coils and blood-stained fluid near its apex. The bony labyrinth soon becomes involved in the inflammatory process, and necrosis of a variable extent of the capsule is very liable to occur. In one of the cases there was very extensive necrosis of the osseous labyrinth, and it is not uncommon to find sequestra in its outer wall during the course of the radical mastoid operation. Tuberculous disease of the middle ear, as before mentioned, is apt to lead to early and extensive destruction of bone; the disease does not always extend to the labyrinth, but a mixed infection is apt to invade the latter through an opening made by the tuberculous process. Extension to the brain or meninges is more liable to occur in the acute than in the chronic form owing to the more rapid progress of the disease in the former, and also to the fact that

granulation tissue formation, which tends to limit the extent of the infective process, is not so marked.

The chronic form may be chronic from the commencement, or it may follow the acute variety. It also may be localized or diffuse. It is usually accompanied by extensive formation of granulation tissue, and on opening the labyrinth the presence of suppuration is recognized more by the presence of granulations than of pus. The former may often be observed protruding from fistulæ in the bone or from perforations in the oval or round windows. In one case the canalicular labyrinth was filled with granulation tissue, while in two others the whole of the internal ear was in a condition of chronic granulating labyrinthitis. One case of tuberculous labyrinthitis occurred in which the internal ear was filled with pale granulations which also protruded through the foramen ovale. The bone is often the seat of extensive necrosis, and sequestration of one of the chambers alone, or even of the whole of the internal ear, is sometimes met with. Cholesteatoma is commonly associated with chronic disease of the labyrinth, and it appears to be specially frequent in connexion with fistulæ of the external semicircular canal.

In the acute form the labyrinth may be packed with masses of round-cell infiltration in which the presence of micro-organisms may sometimes be demonstrated. Micro-organisms also may occasionally be found in the substance of an intact fenestral membrane. The inflammatory exudation, though usually diffuse, may be limited to one part of the labyrinth; thus, in one case, the first half-turn of the cochlea was alone affected.

In a typical case of acute diffuse labyrinthitis the scala vestibuli and scala tympani were filled with masses of round cells which were also found in the lacunar spaces of the modiolus. In those cases in which the auditory nerve is involved, if a section of the petrous bone be cut so as to pass through the cribriform plate of the fundus of the internal auditory meatus, the spiral ganglia and nerve-fibres may be found to be infiltrated with round cells. The blood-vessels in the affected portion of the labyrinth are dilated and engorged.

The pathways of infection from middle to internal ear. — The labyrinth may become infected as the result of a traumatic perforation of the capsule, but more commonly as a result of infective middle-ear disease. The former class of case may be due to a fracture of the base of the skull involving the petrous bone. During the past fourteen years ten cases of this form of fracture, leading to meningitis, occurred, but

I cannot find any mention in the notes as to whether the labyrinth was infected or not. Infective labyrinthitis occasionally results from unskilful attempts to remove foreign bodies from the ear, or during the course of a radical mastoid operation from perforation of the capsule, either intentionally or otherwise, by some instrument. Again, a dislocation of the footplate of the stapes during the operation of curetting the tympanic cavity has been responsible for infection of the labyrinth in a few cases. Many more cases, however, are secondary to infective disease of the middle ear.

Labyrinthitis secondary to infective otitis media.—West and Scott, in a paper on the "Operative Surgery of the Labyrinth" [16], published the results of an investigation into the pathways of infection from the middle to the internal ear. They collected a series of cases—twenty-six in all—which had been under their observation in the Aural Department of St. Bartholomew's Hospital, in which the point of infection had been noted during the course of the radical mastoid operation. Their results are as follows:—

Fistulæ of external semicircular canal	11 cases
,, fenestra ovalis	5 ,,
,, promontory	5 ,,
,, fenestra rotunda	1 ,,
,, external canal and fenestra ovalis	1 ,,
Site unknown	3 ,,

Of the twenty-six cases, eleven were associated with cholesteatoma and in six of these there was a fistula of the external canal only, in one a fistulous canal accompanied destruction of the footplate of the stapes, and in two there was isolated destruction of the footplate of the stapes. I have collected thirty-six cases from the same source, which occurred subsequently to these cases, and thus a series of sixty-two consecutive cases is obtained. In all of them labyrinthitis, either localized or diffuse, was present. In my thirty-six cases the paths of infection were as follows:—

Fistula of external semicircular canal	19 cases
,, fenestra ovalis	4 ,,
,, external canal and fenestra ovalis	5 ,,
,, promontory	2 ,,
,, fenestra rotunda	4 ,,
,, foramen ovale and rotundum	1 ,,
,, superior and external canals	1 ,,

Cholesteatoma was present in eleven cases, and in eight of them it was associated with a fistula of the external semicircular canal alone,

while in three a fistulous canal accompanied a fistula of the oval window. Taking both series of cases together, we obtain the following result :—

Fistula of external semicircular canal	30 cases
,, fenestra ovalis	9 ,,
,, promontory	7 ,,
,, external canal and fenestra ovalis	6 ,,
,, fenestra rotunda	5 ,,
,, superior and external canals	1 ,,
,, foramen ovale and rotundum	1 ,,
Site unknown	3 ,,

Cholesteatoma was present in twenty-two cases, in eighteen of which fistula of the external canal was present.

Hinsberg [5], in a paper on this subject, collected a comparatively large number of cases, namely 198, but the point of entrance of the infection could only be discovered in sixty-one cases. His results were very similar, they were as follows :—

Fistula of external semicircular canal..	27 cases
,, fenestra ovalis	17 ,,
,, promontory	7 ,,
,, in other canals	5 ,,
,, of fenestra ovalis and rotunda	3 ,,
,, fenestra rotunda	3 ,,

Brieger [1] considers that lesions of the fenestral membrane transmit infection to the labyrinth more frequently than fistulæ of the semicircular canals. He states that in four cases of labyrinthine suppuration out of five, infection entered through the foramen rotundum.

It is not, however, essential that there should be an actual fistula in the outer wall of the labyrinth for the latter to become infected from the middle ear. Scott has published a case [11] in which no path of infection was evident to the naked eye. As symptoms pointing to labyrinthitis were present, an operation was performed to examine the outer wall of the labyrinth. No path of infection in the latter could be discovered, the stapes was in position and the promontory of the cochlea and eminence of the external semicircular canal were not fistulous or eroded. The mucosa in the fossula rotunda and in the sinus tympanicus was greatly swollen. The patient died two days later, and at the *post-mortem* examination localized meningitis was found around the pons and medulla, with excess of cerebrospinal fluid in the lateral ventricles of the brain. There was no other evidence of any path of infection in the base of the skull. Sections of the petrous bone were afterwards cut and the labyrinth was found to be in a state of diffuse round-celled infiltration and to contain masses of polymorphonuclear cells and long-

chained streptococci. Serial sections through the fossula rotunda showed cocci among the cells in the mucosa, in the fenestral membrane, and in the cochlea. The membrane was partly ulcerated, but there was no actual perforation. In this case, therefore, the internal ear became infected through the fenestra rotunda, without any actual opening through its outer wall being present.

Extension of infection from the labyrinth to the meninges.—All the pathways from the labyrinth lead into the posterior cranial fossa, with one exception, namely, a perforation in the anterior crus of the superior vertical canal, in which case the middle fossa may be infected. If infection extends beyond the dura into the intradural space, circumscribed or diffuse meningitis or cerebellar abscess will result. Infection may rapidly spread to the meninges, especially if the lesion be an acute one, or more slowly if it is of a more chronic nature.

Although the course of tuberculous disease of the middle ear is slow, yet, if secondary infection by some pyogenic organism occurs, an acute and rapidly fatal meningitis may result.

Extension of the labyrinthine disease usually follows normal openings in the bone for the auditory nerve and aqueducts of the vestibule and cochlea, infection through the internal auditory meatus being most common. In five of the twelve cases infection spread along the eighth nerve; in the remaining cases, although no note was made as to the condition of the nerve, there was no other obvious lesion. The nerve may be greatly inflamed, and in one case microscopical examination revealed round-celled infiltration of the nerve as it entered the internal auditory meatus. There may be plastic adhesions of lymph around the eighth nerve, or the arachnoid sheaths of the seventh and eighth nerves may be distended with turbid fluid or even pus. The internal auditory canal may contain lymph, thick yellow fluid or pus. The pia-arachnoid in the neighbourhood of the internal auditory meatus may be thickened and adherent to the dura. The arachnoid tissue may be distended with turbid fluid and pus, and in one case there was a cystic collection of fluid around the intracranial portion of the seventh and eighth nerves.

Extension through the aqueductus vestibuli will give rise to an empyema of the saccus endolymphaticus, and infection may spread to the meninges from the latter. An empyema of this sac is not a common sequel to labyrinth infection, since the aqueduct is an extremely minute canal and its lumen is liable to become obliterated by the formation of granulation tissue. Moreover, the arachnoid sheath of the seventh and eighth nerves offers a much easier route for the spread of infection.

One case of an empyema of the saccus endolymphaticus of a doubtful nature has been included among the cases of extradural abscess, since, as previously mentioned, it is impossible to distinguish between an empyema of the sac and a post-tympanic extradural abscess without a histological examination of the labyrinth, and this examination, unfortunately, was not carried out in this instance.

Extension through the aqueductus cochleæ may possibly cause lateral sinus thrombosis, for the aqueduct transmits a small vein which drains into the lateral sinus. Infection of the meninges may possibly occur by this channel, but if so it appears to be extremely rare.

Labyrinthine suppuration may open up new pathways of infection through the capsule. Thus erosion of the superior canals might give rise to an extradural abscess, or possibly to meningitis by direct extension without the formation of any abscess.

Hinsberg [5] reports 198 cases of labyrinthine infection, the cranial cavity being infected in 108. In 43 the pathway of infection could be traced, viz. :—

Through the internal auditory meatus	.. ..	25 cases
,, ,, ,, ,,	and aqueductus vestibuli ..	1 ,,
,, aqueductus vestibuli	.. ..	8 ,,
,, ,, cochleæ	.. ..	1 ,,
,, fistulæ in vertical canals	.. ..	8 ,,

When considering the subject of meningitis secondary to infective labyrinthitis, it is necessary to bear in mind the fact that the labyrinth can be infected by spread of the disease from the cerebral meninges. In order to demonstrate this it is necessary to examine both petrous bones histologically, and to show that the labyrinths of both sides are affected, or that the middle-ear cavities are not diseased. In one case the bilateral labyrinthitis was secondary to pneumococcal meningitis. In this case there was no obvious middle-ear disease. On the right side the cochlea contained round-celled infiltration and the footplate of the stapes was in position. On the left side the cochlea presented a similar appearance and the footplate of the stapes was also in its normal position. The mucous membrane of the middle ear did not appear to be affected, though in microscopical section it was thicker and more vascular than normal. On both sides round-celled infiltration surrounded the eighth nerve as it entered the internal auditory meatus. In another case a full histological examination of the petrous bone was made. On both sides there was labyrinthitis which was apparently secondary to the meningitis. The tympanum was normal on both sides. In this case the meningitis was tuberculous.

Goerke [2] examined nineteen temporal bones in cases of cerebrospinal meningitis, and found that they were normal in only two cases. In the other seventeen inflammatory changes were present. The path of infection from the meninges was found to be through the aqueduct of the cochlea in three cases, through the aqueduct of the vestibule in one case, and along the auditory nerve sheath in eleven cases. In the other cases the path was doubtful.

Habermann claims that in every case of severe cerebrospinal meningitis, infection and transmission to the labyrinth take place solely through the aqueducts of the cochlea.

Conclusions.—Infective labyrinthitis most often occurs as a result of suppurative disease of the middle ear, and the labyrinth is especially liable to become infected when the otitis media is accompanied by cholesteatomatous formation. The pathways of infection may be divided into three classes:—

(*a*) Fistula of the external semicircular canal, which is by far the most common.

(*b*) Fistulæ in other situations, of which fistulous openings in the oval and round windows and promontory are the most common.

(*c*) Through round windows without any actual perforation of the membranes. This class of case may possibly be more frequent than it has hitherto been considered to be, especially in acute cases.

With regard to the possibility of infection taking place through the aqueductus Fallopii along the seventh nerve to the internal auditory meatus, I have obtained no evidence to prove that this does occur; on the other hand, in several histological sections from Scott's series that I have examined, while the eighth nerve was infiltrated with round-cells, the seventh in its canal was unaffected.

The labyrinth may also be infected from the cranial cavity in cases of meningitis, especially in the cerebrospinal variety, infection spreading along the arachnoid sheaths of the seventh and eighth nerves.

Spread of infection from the labyrinth to the meninges takes place in the great majority of cases along the sheath of the auditory and facial nerves.

It is possible for the septic process to extend to the meninges along the aqueducts, or through fistulæ in the osseous labyrinth, but no cases of this kind occurred and they appear to be extremely uncommon.

The cases of meningitis secondary to pneumonia require no further consideration, since the otitis in all probability was not directly responsible for the meningitis.

With regard to the thirty-nine cases in which the evidence as to the origin of the meningitis was incomplete, it need only be mentioned that, although the labyrinth was most probably the cause of the meningeal infection in several of them, no microscopical examination was made, and therefore the path of infection is uncertain.

Some of the remaining cases were, no doubt, ordinary instances of meningococcal and pneumococcal meningitis, in which the ear-disease was not the direct cause.

Examination of this series shows that cases of otitic meningitis may be divided into two main classes, namely:—

(1) Cases secondary to some gross intracranial lesion, such as extradural abscess, lateral sinus thrombosis and brain abscess, and possibly to perforative disease of bone, and

(2) Cases in which no gross intracranial lesion can be found.

In the first class of case the cause of the meningitis is usually obvious, and the spread of infection takes place from the different intracranial lesions in a variety of ways which have been indicated in the preceding pages. In the second group of cases the path of infection may not be so evident, although in many cases in which the infection has spread from the labyrinth there are indications, such, for example, as patches of lymph round the nerve-sheaths or round the internal auditory meatus, on one side, which point to the source of the meningitis. In this class of case the paths of infection are either vascular or labyrinthine, and of the two the latter is probably the more common.

It is probable that the cause of otitic meningitis unassociated with gross intracranial lesions, is, in the majority of cases, infection from the labyrinth, and that infection spreads from the latter to the meninges by way of the arachnoid sheaths of the auditory and facial nerves.

Chapter V.—General Conclusions.

In this paper I have endeavoured to indicate the possible pathways of infection in the various intracranial complications secondary to infective otitis media, and to determine those which may be considered of most importance.

Infection through vascular channels appears to be responsible for most cases of lateral sinus thrombosis, while vascular infection is a cause of extradural and brain abscesses in a large number of cases.

Many cases of extradural abscess are due to disease of the petrous

bone, especially its posterior surface and tegmen; in those cases where the bone is unaffected, the dura mater becomes infected through a septic endophlebitis of a vein of the tympanic mucosa extending to a vein of the dura. Cerebral and cerebellar abscesses may be due to direct contact of the brain with diseased dura mater; if perforation of the latter takes place, direct extension to the cerebral substance may occur; if no perforation occurs, the disease may spread to the brain by infection of the veins in the dura, with extension from them to the vessels of the pia-arachnoid, and from the latter to the interior of the brain.

Cerebellar abscess is also often secondary to infective labyrinthitis, extension of the disease taking place along the nerve-sheaths, or directly in the region of the posterior semicircular canal.

Leptomeningitis is either (*a*) secondary to a gross intracranial lesion or bone disease, in which case it is due to the rupture of an abscess into the intradural space or to vascular infection from the lateral sinus, abscess, or bone, as the case may be; or (*b*) to labyrinthitis, with infection spreading along the nerve-sheaths, or vascular infection from the middle ear direct.

The results of this investigation show that infection of the labyrinth is responsible for many cases of cerebellar abscess and meningitis of otitic origin. Formerly, disease of the labyrinth, owing to lack of knowledge as to its pathology, did not receive sufficient attention as a cause of intracranial infection. Of recent years, however, our knowledge of the diseases affecting it, and their bearing on the subject of encephalic infection, has increased rapidly.

At the present time, surgeons when operating for disease of the middle ear pay more attention to fistulæ or necrosis of its inner wall as evidence of possible labyrinthine involvement. Moreover, various clinical tests which have been introduced lately, such as the rotation tests and the caloric and galvanic reactions, when taken together, appear to afford a fairly sure means of diagnosing this condition. In this way many cases of labyrinthine infection are discovered which in earlier years would almost certainly have been overlooked.

A considerable number of cases of tuberculous and cerebrospinal meningitis occur in patients with infective ear-disease in which the latter is not the obvious cause of the meningitis, and the question as to whether the ear can be regarded as being the channel of infection in such cases requires to be further investigated.

In conclusion I take this opportunity of thanking Mr. Ernest West

and Mr. Sydney Scott for permitting me to refer to patients who have been under their care. I must also express my gratitude to Mr. Scott for so kindly allowing me to examine his microscopical specimens, and also for much kind advice in the preparation of this paper.

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SOME RARER MANIFESTATIONS OF PARASYPHILIS OF THE NERVOUS SYSTEM.

BY A. READ WILSON, M.D.

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INTRODUCTION.

No sooner was the long dispute, extending over something like thirty years, as to whether syphilis is, or is not, the essential etiological factor in tabes dorsalis and general paralysis of the insane finally settled in the affirmative, than a new contention arose with regard to the exact relationship of these two conditions to each other.

In 1906, however, in his Lumleian lectures on Tabes Dorsalis, Ferrier [12] crystallized the views of most neurologists when he expressed the opinion that tabes and general paralysis are "merely different aspects of the same polymorphic disease."

Fournier [13], to whom more than any other we owe the recognition of parasyphilitic nervous disease—who, indeed, introduced the word—gave a very comprehensive list of affections which, in his opinion, were parasyphilitic.

I.—Acquired syphilis.

(1) Acute hystero-neurasthenia of the secondary period.
(2) Various neurasthenic manifestations of a more advanced stage.
(3) Hystero-syphilis.
(4) Tabes dorsalis.
(5) General paralysis of the insane.

(6) A special form of epilepsy.

(7) A special form of muscular atrophy.

II.—Congenital syphilis.

Numerous dystrophies and malformations; cases of arrested or retarded development; cachexias, non-viability, &c.

Certain cases of simple meningitis in children.

Perhaps some cases of true epilepsy.

Certainly every case of juvenile tabes and juvenile general paralysis.

This is not the whole list, but is sufficient to show that as long ago as 1894 Fournier was regarding parasyphilis as a much wider entity than was generally supposed; in other words, that it included many other manifestations of disease besides tabes and general paralysis and the combination of the two known as tabo-paresis.

Both these conditions are primary progressive nerve-tract degenerations. But there are certain other nervous diseases of this type; and I shall endeavour to show that in some instances they are parasyphilitic, for we meet with them in patients giving a positive Wassermann reaction, whether syphilis is admitted or denied, and we find them more or less frequently, but at all events sometimes, combined with the recognized parasyphilitic manifestations, general paralysis and tabes. The diseases with which I shall concern myself are three in number, viz.:—

Primary Optic Atrophy,

Primary Lateral Sclerosis, and

Progressive Muscular Atrophy.

All these diseases are of the same primary character—a degeneration of neuronic groups. Tabes dorsalis is the manifestation of a degeneration of the spinal sensory protoneurons; general paralysis, of the cortical association neurons; primary optic atrophy, of the visual neurons; primary lateral sclerosis, of the upper motor neurons; progressive muscular atrophy, of the lower motor neurons.

In the case of tabes and general paralysis the essential etiological factor is the same, syphilis; the old oft-quoted alternative factors, "alcohol, hard work, exposure," are the same; the average interval between infection with syphilis and the declaration of symptoms is the same; the average age-incidence is the same; the symptoms and termination are analogous; signs of gross syphilitic lesions are infrequent, since both usually follow mild attacks of syphilis; and the two diseases are frequently combined in one individual. Moreover, both may attack the subjects of either acquired or congenital syphilis.

Some cases of primary optic atrophy, primary lateral sclerosis, and

progressive muscular atrophy show an extraordinary analogy to the above—extraordinary, that is, if they are to have a different etiology, but natural enough if considered as parasyphilitic manifestations. Many give histories of syphilis, others have signs of syphilis remaining on their bodies, or they give positive Wassermann reactions. Evidences of gross syphilitic lesions, too, are rare, since the primary stages have in most cases been mild. Alcohol, hard work and exposure are again amongst the most commonly accepted etiological factors. The average interval between syphilitic infection and the appearance of symptoms is about the same as in tabes or general paralysis. The average age incidence is the same, though in primary lateral sclerosis the onset is so gradual that the patients do not seek advice at the commencement. All three are frequently found associated with tabes, less often with general paralysis; cases occur where two of them are associated together, or where multiple combinations are exhibited. About 10 per cent. of general paralytics have tabes too (Byrom Bramwell, [4] Mott [30]); some 4 per cent. of general paralytics have primary optic atrophy (Mott [30]); primary optic atrophy is found in from 10 per cent. (Osler [40]) to 20 per cent. (Norris and Oliver [38]) of tabetics; and 20 per cent. of tabetics exhibit some form of muscular atrophy (Dejerine [8]). Further, undoubted examples of juvenile primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy exist.

I have recently seen it suggested that, although the neuronic degeneration in progressive muscular atrophy is essentially similar to that in tabes, it is rather to be laid to the account of a "yet-to-be-discovered toxin" than to that of syphilis. This is somewhat like setting up an altar to an unknown god—a proceeding natural enough for the philosophers of ancient Athens, but to be deprecated in an age of exact science. A man proved to have committed a certain crime must necessarily be suspected when that crime is exactly reproduced, but failure definitely to bring it home to him is no justification for hanging someone else about whom nothing is known. If the lesions found in progressive muscular atrophy were utterly unlike those produced by any agent of disease yet known to us, an "undiscovered toxin" would be as fair and scientific an hypothesis as Halley's, when he deduced the orbit of the comet which bears his name and predicted the date of its return.

Syphilis is known to be the cause of a vast amount of disease; it is even said that it enters into the etiology of one-third of all the

disease of the world, and investigations which are being carried out in Australia under the Victorian Government, reported by Dr. J. W. Barrett, of Melbourne, in a paper recently read before the Royal Society of Medicine, tend to confirm this. This disease has been shown to be the essential cause of the two most common primary nerve-tract degenerations, and it is fair, therefore, to suspect it in diseases where the pathological conditions found after death are on all fours with those of degenerations of established syphilitic origin, as is the case with most examples of primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy.

With regard to the sex-incidence of parasyphilis the proportions given by different compilers of statistics vary between three to one and twenty to one in favour of males. No doubt truth lies between. At all events more men are smitten with parasyphilis of the nervous system than women. Why this should be so is an interesting study. Beyond question more men acquire syphilis than women. A young man contracting the disease from a prostitute, as is often the case, is naturally unable to infect so large a circle as she has the opportunity of doing. When he does pass the infection on the recipient is very probably a member of the same class as the first, and becomes another centre of dissemination for the male sex. So we can only expect to find the disease commoner in men than women. Does this account for the whole discrepancy between the sexes with regard to parasyphilis? Probably not. In the first place, a large proportion of prostitutes never reach the parasyphilitic age. Secondly, very many women who marry syphilized men are protected by Colles' law. The explanation which is often advanced that women are not so liable to contributory causes is not, I think, a sound one: partly because I do not believe contributory causes play a sufficiently large part in the etiology, and partly because the great majority of women are exposed to stress or strain just as frequently as men, though such stress may take a different form.

The sex-incidence in congenital parasyphilis is of course equal. Still [50] finds that in the cerebral palsies of children the number of boys attacked is to the number of girls as three is to two.

	Boys	Girls
Infantile hemiplegia	32	19
Spastic paraplegia	14	12
,, diplegia	14	8
,, monoplegia	1	0

It will be seen that in spastic paraplegia the sex-incidence is almost the same; and this may be significant with regard to congenital syphilis.

I shall not attempt to prove that every example of primary optic atrophy, primary lateral sclerosis, and progressive muscular atrophy is parasyphilitic. Primary optic atrophy undoubtedly occurs as a sequela or complication in lead poisoning, some specific fevers, diabetes; yet it is not an invariable complication, and investigation may conceivably show that it is only manifested in persons who have a congenital or acquired syphilitic taint. Also, up to the present, so few cases, comparatively, of primary lateral sclerosis or progressive muscular atrophy have been proved to be parasyphilitic. Even in tabes, where the percentage of unquestionable parasyphilis is so high as 90, the other 10 per cent. are not proven; and, until they are, one cannot deem unreasonable those who suppose that some other agent may possibly, though very rarely, cause progressive bilateral degeneration in the posterior columns of the cord. For if one poison—to wit, the virus of syphilis—can produce the disease, why should not another under favourable conditions occasionally do the same?

I do not therefore attempt to gather every case of primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy into the parasyphilitic net. But the analogies to tabes and general paralysis, together with the fact of their frequent occurrence in combination with these diseases, constitute strong evidence that at all events some cases are parasyphilitic in character. From time to time articles appear in the literature in which the connection of syphilis with these three diseases is recognized and brought out. Thus Mott [31] brackets together general paralysis of the insane, tabes and primary optic atrophy, and describes them as "really a single morbid entity, owning one cause, with an insidious onset, progressive in character, and uninfluenced by anti-syphilitic remedies—in fact, a primary neuronic dystrophy. They may occur successively or simultaneously in the same individual." And again, "It is probable that Erb's spinal paralysis and certain cases of amyotrophic lateral sclerosis may be primary post-syphilitic dystrophies."

The recognition of progressive muscular atrophy as a parasyphilitic manifestation is much further advanced on the Continent, particularly in France, than in England. Fournier [13] placed a "special form of muscular atrophy" in his classification of parasyphilitic affections. Other observers who have published cases to show the parasyphilitic nature of progressive muscular atrophy are Poussard [43], Leri [25], Camus [5], Lannois et Poret [24], van Gehuchten [15], Merle [27], Kinnier Wilson [53], Rose et Rendu [46]. The last-named authors

point out that amyotrophies in tabes, due to peripheral neuritis, affect the lower limbs, whereas those of central origin have a preference for the upper extremities, though the legs are not exempt. In the arms the type is usually that of Aran and Duchenne, or else the shoulder-girdle is most affected. As a rule the degeneration is symmetrical, though one side may be more advanced than the other. Raymond [45] recorded the case of a man who, eleven years after syphilitic infection, suffered from lightning pains in the right shoulder, and four years later developed a progressive atrophy in the muscles of the right hand, spreading to the arm and shoulder. In the following year the left arm was similarly attacked. The muscles at the back of the neck were atrophied equally.

Most of my material has been collected in the various departments of Guy's Hospital, and the laboratory tests have been carried out by the bacteriological department according to Wassermann's original method, except that the rabbits are immunized against human instead of sheep's corpuscles. But I am also indebted to Dr. T. E. K. Stansfield for permission to investigate patients with general paralysis in the London County Asylum at Bexley. In those cases the cytological examination of cerebrospinal fluids, together with the butyric acid, ammonium sulphate and sodium glycocholate precipitation tests, were carried out by Dr. George Evans; whilst the Wassermann tests were all undertaken at Claybury by Dr. J. P. Candler, who also follows the original method, except in the source of the corpuscles, ox blood being used instead of sheep's.

Chapter I.—The Cerebrospinal Fluid and the Wassermann Reaction.

It is unnecessary here to enter into the details of the composition of cerebrospinal fluid, or of the technique of the Wassermann reaction, either in its original form or the modifications introduced by Hecht or Fleming. Neither is it requisite to trace the steps by which the original explanation of the reaction was shattered, nor to enter the discussion as to whether the reaction is, or is not, infallible. All I will say is that the test is probably specific for syphilis and parasyphilis (for though certain cases of malaria give it, malaria is not clinically liable to be confounded with syphilitic disease); yet it does not indicate the organ affected.

If the central nervous system is not affected the reaction will usually be positive with the serum, and negative with the cerebrospinal

fluid. This is natural when we remember that the latter is essentially a secretion. But even in general paralysis the cerebrospinal fluid is very occasionally negative, whilst the serum is positive. Plaut [42] tested both fluids in ninety-five cases of general paralysis, and got a positive reaction with the serum in every case, and in all but one with the cerebrospinal fluid.

In syphilis and parasyphilis there is marked lymphocytosis of the cerebrospinal fluid. This ebbs or flows along with the activity of the disease, and is therefore useful as an index not only to that activity or quiescence, but to the effect of antisyphilitic remedies, whose exhibition in parasyphilis produces no good effect on the disease, and no effect on cerebrospinal lymphocytosis; but in syphilitic meningitis, for instance, as the patient recovers so the lymphocytosis decreases. This lymphocytosis occurs in some other diseases, e.g., sleeping-sickness and herpes zoster, and so cannot be considered absolutely pathognomonic; but its presence is a valuable sign when combined with other facts.

Chapter II.—Forms assumed by Parasyphilis of the Nervous System.

A vast amount of evidence had to be presented by Fournier [14], Gowers [16], Erb [10], in particular, and others before the medical profession accepted the dicta "no syphilis, no tabes," and "no syphilis, no general paralysis of the insane." No such voluminous evidence is forthcoming with regard to primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy. These are very much rarer manifestations, and, not being considered parasyphilitic, more attention has been paid etiologically to alcohol, exposure, and particularly to hard work than to syphilis. Many reports do not mention syphilis at all, or pass it over lightly with "No history of syphilis was given," and very few cases as yet have been subjected to the Wassermann test. When, however, there are signs of tabes or general paralysis in conjunction, syphilis is inquired after carefully and the blood is tested.

Before tabes or general paralysis were recognized as parasyphilitic, the percentage of cases giving a history of syphilis was quite low; but when Fournier, Gowers and Erb were insisting on its etiological importance the figures of competent observers jumped up in a surprising manner. For instance, Bernhardt's [3] rose from 21 per cent. to 60 per cent.; Oppenheim's [39] from 17 per cent. to 80 per cent.; and Rumpf's [47] from 65 per cent. to 80 per cent. The same thing

occurred with general paralysis; and it might well be true of the others, were more care taken in the investigation of histories. Not long ago a case of suspected amyotrophic tabes was brought before the Neurological Section of a certain learned society. The patient was 36 years old and gave a positive Wassermann reaction. She had obvious tabes, and in addition wasting of the small muscles of the hands, particularly the left hand. The patient was a charwoman, and the Section came to the conclusion that the muscular atrophy was due to her occupation, explaining the more advanced condition of the left hand as due—upon what grounds I know not—to greater pressure upon that hand in the process of scrubbing floors.

If one group of neurons can degenerate as a result of antecedent syphilis, why not another group, or any other? If both tract degenerations can be explained as parasyphilitic in tabo-paresis, why not in tabes combined with progressive muscular atrophy? Yet we find constantly this seeking for a separate and distinct cause in cases where either tabes or general paralysis are combined with some other tract degeneration.

Of all the conditions of degeneration which, rightly or wrongly, have been laid to the account of syphilis by different writers, I propose to confine myself to pure instances of primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy, and combinations of these, either with each other or with tabes or with general paralysis. If any of the other suggested parasyphilitic manifestations are mentioned they will only be referred to incidentally, except in the case of tabo-paresis, which I shall take as the prototype of the coincidence in one individual of two separate parasyphilitic tract degenerations.

My subject can therefore be divided into the following two sections with fourteen subsections :—

(I) *Uncomplicated.*
- (*a*) Primary optic atrophy.
- (*b*) Primary lateral sclerosis.
- (*c*) Progressive muscular atrophy.

(II) *Complicated.*
- (*d*) Tabes combined with general paralysis.
- (*e*) Tabes combined with primary optic atrophy.
- (*f*) Tabes combined with primary lateral sclerosis.
- (*g*) Tabes combined with progressive muscular atrophy.
- (*h*) General paralysis combined with primary optic atrophy.
- (*i*) General paralysis combined with primary lateral sclerosis.

(*j*) General paralysis combined with progressive muscular atrophy.

(*k*) Primary optic atrophy combined with primary lateral sclerosis.

(*l*) Primary optic atrophy combined with progressive muscular atrophy.

(*m*) Primary lateral sclerosis combined with progressive muscular atrophy.

(*n*) Cases where more than two of the symptom-groups are manifested in one individual.

Some of these are comparatively common affections, others are rare, and although I cannot cite an actual case of primary optic atrophy combined with progressive muscular atrophy, there is no theoretical reason why it should not exist.

In each of these there is a definite degeneration in brain or cord, or nerve-trunk, which can be anticipated from a knowledge of the symptoms, and can be demonstrated *post-mortem*.

In (*a*) there will be degeneration of the optic nerve alone.

In (*b*) there will be degeneration of the upper motor neurons.

In (*c*) there will be degeneration of the lower motor neurons.

In (*d*) there will be degeneration of the spinal sensory neurons and of the cortical association neurons.

In (*e*) there will be degeneration of the spinal sensory neurons and of the optic nerve neurons.

In (*f*) there will be degeneration of the spinal sensory neurons and the upper motor neurons.

In (*g*) there will be degeneration of the spinal sensory neurons and of the lower motor neurons.

In (*h*) there will be degeneration of the cortical neurons and of the optic nerve neurons.

In (*i*) there will be degeneration of the cortical neurons and of the upper motor neurons.

In (*j*) there will be degeneration of the cortical neurons and of the lower motor neurons.

In (*k*) there will be degeneration of the optic nerve and of the upper motor neurons.

In (*l*) there will be degeneration of the optic nerve and of the lower motor neurons.

In (*m*) there will be degeneration of both the upper and lower motor neurons.

In (*n*) there may be degenerations of any combination of these tracts.

The decay of the affected tract may be rapid, as in primary optic

atrophy or general paralysis of the insane; or slow, as in tabes, primary lateral sclerosis or progressive muscular atrophy.

Norris and Oliver [38] give the average length of time for primary optic atrophy to progress to total blindness as about one year—it varies from a few months up to fifteen years. General paralysis usually ends fatally in from two to three years. The other three conditions may drag on very much longer.

It has been remarked that when two parasyphilitic manifestations are present in one individual, there is a tendency for the disease to progress more slowly. Benedikt [2], as long ago as 1881, pointed out that primary optic atrophy coming on in the pre-ataxic stage of tabes exercised a favourable influence, and retarded the symptoms. If this amelioration of the symptoms of one tract degeneration produced by the coincidence of a second is a reality, it might tend to show that both the degenerations were due to one cause. For if two totally distinct causes were at work there could be no reason why one should be favourably affected by the other, whereas if one virus were, so to speak, dividing its attention between two or more tracts it might be argued that it would have less energy to devote to either one of them, and so each would be retarded.

Some, if not all, of these conditions may be simulated by active syphilis; for example, a man may have the signs and symptoms of spastic paraplegia with a history of syphilis and a positive Wassermann, and yet under the influence of antisyphilitic remedies the condition clears up; thus proving that the condition was syphilitic (*i.e.*, gummatous, or due to syphilitic meningitis) and not parasyphilitic. Parasyphilis is unaffected by the antisyphilitic remedies, namely, mercury and potassium iodide; but whether it will be found that it is amenable to salvarsan injections the evidence at our disposal is at present insufficient to determine. Amongst the cases recorded later there is one (Case 19) entirely unaffected by mercury and potassium iodide, which, after salvarsan injection, gave a negative Wassermann, though the reaction was positive before. The interval, however, in this case between the injection and the change in the Wassermann reaction was so short—only two weeks—that perhaps it is of no importance. It might by itself be looked upon as a hopeful indication, seeing that it has been considered a rule that, although parasyphilis may not at first give a positive Wassermann, when in the progress of the case the reaction has once become positive the patient does not afterwards give a negative one.

A general distinction between a true and false parasyphilitic manifestation may be drawn thus:—

Parasyphilis.	*Pseudo-parasyphilis.*
(1) First symptoms not generally noticed till eight to fifteen years or longer after primary infection.	(1) First symptoms noticed less than eight years, and often very soon, after primary infection.
(2) Average age-incidence 37 years.	(2) Very many patients are under 25 years of age.
(3) Begins usually after all syphilitic manifestations have disappeared.	(3) Tertiary or late secondary manifestations may co-exist.
(4) Onset insidious as a rule and progress not very rapid.	(4) Onset often sudden, often determined by an accident, as a fall or a blow, and progress rapid.
(5) History of syphilis as a rule shows few and mild early symptoms.	(5) History of syphilis often shows a severe attack.
(6) Reaction to antisyphilitic remedies *nil*, or injurious.	(6) Reaction to antisyphilitic drugs marked and beneficial.

Head [19] suggests that in spinal cases where the onset is sudden the prognosis is bad. But in parasyphilis the prognosis is bad whether the onset be sudden or slow. In syphilitic disease of the cord the prognosis depends more upon the lesion than upon the suddenness or otherwise of the attack. In thrombosis and hæmorrhage the onset is likely to be most sudden, and certainly in such the prognosis is grave, for it is difficult to see how antisyphilitic or any other remedies are going to remove thrombus or clot, at all events in time to prevent permanent damage to the nervous elements from softening or compression. But in cases where the symptoms are due to gumma, or thickening of meninges, recovery is by no means rare under antisyphilitic treatment.

Wassermann's test is of great value in the differential diagnosis of parasyphilis and pseudo-parasyphilis, as the following three cases mentioned by Mott [29] indicate.

(1) A woman was admitted to an asylum as a general paralytic; she exhibited cerebrospinal lymphocytosis, but the Wassermann reaction was negative. Under treatment by mercurial inunction the symptoms of general paralysis cleared up.

(2) A man was admitted to an asylum as a general paralytic. He improved so greatly that he would have been discharged as cured but for the fact that his cerebrospinal fluid gave a positive Wassermann

reaction. Suddenly he began to have seizures and died. *Post-mortem* his brain showed lesions of general paralysis of the insane.

(3) A woman with definite tabetic symptoms, but who had probably been infected less than four years before, showed intense cerebrospinal lymphocytosis, but a negative Wassermann reaction. The symptoms cleared up under mercurial inunction. This case shows the value of giving anti-syphilitic treatment a trial in apparent parasyphilis of the nervous system when the Wassermann reaction is negative.

It is commonly said, and observation tends to confirm the view, that parasyphilitic nervous disease as a rule follows an apparently mild attack of syphilis. If, however, we consider the terminal nervous degeneration as really an ultimate part of the attack, it cannot in its totality be described as mild. Mott [32] quotes Fournier as saying that: "If the virus expends itself in severe primary or secondary manifestations there is less tendency to parasyphilis afterwards," and Mott, himself, was surprised at the rarity of tertiary lesions in over 500 *post-mortem* examinations on general paralytics. He says, further, that in spite of the well-known debauchery and sexual promiscuity of many general paralytics in the early stage of the disease, he has never seen a primary sore or secondary rash on such a patient. Krafft-Ebing [23] confirms this observation, and put it, as well as the "no syphilis—no general paralysis" dictum, to a severe test; he selected nine patients suffering from general paralysis of the insane who gave no history of syphilis and who had no physical signs of the disease about their bodies, and inoculated them by injecting the virus from a typical hard chancre; none of them developed syphilis, showing that they had become insusceptible to the disease.

Syphilis established in a race tends to produce racial syphilization with consequent inherited insusceptibility, and, as a result, we see fewer cases of severe syphilis than in former generations. Yet there are more cases of tabes and general paralysis. May this not be because the population increases, and consequently there are more cases of syphilis than formerly, although of a milder character, parasyphilitic degenerations being more apt to follow mild attacks in which the virus has not spent itself riotously in the early stages?

Why do the effects of syphilitic inoculation differ so widely? Why should the disease in one patient, with apparently a mild attack, lead, after a period of entire quiescence, to such grave and devastating degenerations of the nervous system, while another, with what appears a far more severe infection, develops no nervous symptoms in after

life at all? Is the difference in the *Spirochæta pallida* or in the patient's resistance, the defensive reaction excited in the tissues by the presence of the virus? And, if it is a question of resistance, is it the resistance of the organism as a whole or of the individual tissues? Comparison with malaria indicates the possibility of the existence of varieties of the spirochæte. Or the virus may be modified by passage through certain individuals, or the treatment of the disease may modify the virus. This last, however, is hardly likely, seeing that precisely the same ultimate nervous degeneration may overtake a man who never had any treatment with mercury at all as one who underwent a prolonged course; unless we allow that the mercurial modification of the virus occurred during passage through a previous individual. The following remarkable instances, quoted by Mott [33], point strongly in the direction of there being at all events a special neurotoxic variety of the spirochæte, or a special neurotoxic modification of the virus.

Two students were infected with syphilis on the same day by the same woman; both died fifteen years later of general paralysis (Babinski). Two men were infected with syphilis about the same time by the same nurse; both were general paralytics ten years afterwards (Mott). Two men acquired syphilis from the same source about the same time; ten years later both were subjects of tabes dorsalis (Marie and Bernard). Four men were infected with syphilis by one woman, and later all suffered from either tabes or general paralysis; a fifth man who also had connexion with this woman, but did not contract syphilis, did not develop either tabes or general paralysis (Erb). Seven glass-blowers were under treatment together for chancre of the lip. Ten years later five of them came under observation, and four were suffering from tabes or general paralysis (Brosius). This extraordinary example is given by Morell-Lavallée [28]:—

Marthe X., in 1870 the mistress of Primus (medical student); he died in 1873 of syphilitic meningitis.

In 1871 she was the mistress of Secundus (medical student); he married later and had healthy children, but died in 1888 from general paralysis.

In 1872 the mistress of Tertius (medical student); he married later and had two healthy children, but died in 1882 from general paralysis.

Later the mistress of Quartus (chemist); he died in 1890 from general paralysis.

Later the mistress of Quintus (engineer); he died of "folie syphilitique." The whole five being infected with syphilis by this woman.

Yet experiments on animals do not uphold the theory of variation in the spirochæte, or of modification of the virus so as to be specially toxic to given tissues; for there appears to be no difference in the lesions produced by inoculating apes with virus obtained from a wide range of syphilitic lesions. And a chimpanzee inoculated with virus from a syphilized monkey (*Macaque*)—which does not react well to the disease, and might, therefore, be supposed to modify the virus by passage—shows similar and equally severe lesions as one inoculated directly from a human subject. Therefore, until further light is thrown on the question, we must consider that the variations in the symptom-complex are due, not to the virus but to the differences in resistance of the individuals attacked—difficult as it undoubtedly is to explain the above quoted instances simply as coincidences.

Profeta's law, that a non-syphilitic child of a syphilitic mother does not acquire syphilis from the syphilitic mother who suckles it; and Colles' law, that a non-syphilitic mother does not contract syphilis when suckling her syphilitic child, whereas a wet nurse does, show that immunity is attained by the child or mother acquiring some antitoxic substance from the other.

In a large number of cases of congenital general paralysis, Mott [34] obtained a history of frequent miscarriages in the mother and of her bearing typical syphilitic children, without herself acquiring the disease. In two instances the mother died of general paralysis, whilst a considerable number of the fathers succumbed to this disease. The usual conjugal history of the parents of juvenile parasyphilitics is of this type: First a longer or shorter series of miscarriages; then children born dead, and children dying in infancy—often from hydrocephalus or meningitis; then children apparently healthy, but who later show premature nervous decay, suffering for example from nerve deafness, optic atrophy, tabes or general paralysis; and finally healthy children, indicating either that in the course of time the virus becomes attenuated, or that the resistance of the offspring increases in strength, or that both these processes are in operation together. Occasionally, however, a child with signs of inherited syphilis, or a parasyphilitic child, may be born out of its turn as it were, after several healthy ones. Levaditi has actually observed the *Spirochæta pallida* within the ovum, and the phenomenon may be explained by the virus attacking one ovum and not another, or by this particular ovum having less resistance than previously fertilized ones.

How can the degeneration of particular groups of neurons be

accounted for? Why should one parasyphilitic individual suffer from tabes, another from general paralysis, others from primary optic atrophy, primary lateral sclerosis or progressive muscular atrophy, or others from combinations of two or more of these together? In direct syphilis of the nervous system the particular position of the lesion is probably fortuitous, there being an accidental metastasis of the organism at that spot. This cannot be the case in parasyphilis, for though a variety of symptoms may be present, yet the very constant occurrence of the Argyll-Robertson pupil—which is probably only met with in parasyphilis of the nervous system—shows that the incidence cannot be random and uncontrolled. Neither spirochætes nor antigens have ever been demonstrated in the cerebrospinal fluid (though inoculation of apes with that fluid is said to have been followed by the development of syphilis); but antibodies are found, or at least the unknown substance which acts the part of antibody in Wassermann's reaction, and probably in direct proportion to the neuronic decay. Nerve-cells are not capable of regeneration, though their processes are; and when decay sets in it begins in the dendrites and travels back finally to the cell and its nucleus. Most infections are short lived and fleeting in effect, and the tissues attacked are not usually so injured as to preclude recovery sooner or later. But syphilitic infection is unfortunately prolonged, at the best severe, and the individual attacked never knows when he is at the end of his troubles; often it lasts till the end of the victim's life, and very frequently either directly or indirectly brings about his death. When such a prolonged evil influence is brought to bear on nervous tissues it leads to permanent and irreparable damage—premature decay and death.

Bacterial infections may be important in determining the locality of parasyphilitic degeneration, by lowering the resistance of one group of neurons more than another, and they may also be the immediate factor in the onset of the disease, or produce aggravation of symptoms and acceleration of decay. Parasyphilitics not only readily fall victims to microbic infections, but are especially liable to be carried off by them, or to show increased rapidity in the progress of the disease as a result of such attack. Possibly the toxic effects of secondary bacterial infections are greatly increased by the presence of the increased quantity of lipoids in the blood, consequent on the nervous decay.

The Argyll-Robertson pupil is the most constant physical sign of parasyphilis of the nervous system and occurs rarely in diseases that are due to syphilis or its sequelæ. Babinski pointed out that the

phenomenon of the Argyll-Robertson pupil is not confined to tabes or general paralysis, but may be found in other post-syphilitic states.

It may well be, when in course of time parasyphilitic manifestations come to be more fully recognized and classified, that the Argyll-Robertson pupil will hold the first place as the commonest of them all. Whether it ever occurs as the only sign is difficult to determine —patients do not seek advice for loss of light reflex. It is so commonly found with tabes, general paralysis, and primary optic atrophy, as to be regarded as a symptom of all three ; but in the case of tabes, at all events, it is difficult to see how degeneration of the ciliary ganglion can be in any way the result of degeneration in the posterior columns of the lower cord, and yet the Argyll-Robertson pupil is often found so early in the disease that the only other sign may be an absent tendo-Achillis jerk. It is more easy to understand the ganglion degeneration as a concomitant of the spinal degeneration, owning a common cause with it, than as its result. Similarly, in general paralysis with the phenomenon, both are probably separate manifestations of a primary condition. With primary optic atrophy, if the pupil light reflex were not lost till after blindness had occurred, it might be argued very fairly that it was due to the non-perception of the light stimulus, but it is found before vision is lost. Here again we may have two results of one protean disease.

The motor nerves of the extrinsic ocular muscles are frequently affected in parasyphilis, producing ptosis and various ophthalmoplegias. These may be due to a peripheral neuritic condition; but in some cases where the paralysis does not vary, as it does in the neuritic ones, the disorder may be due to a lower neuron degeneration, a parasyphilitic progressive muscular atrophy in fact. Merely a different aspect of the same polymorphic disease.

If a number of the different groups and systems of neurons of which the central nervous system is made up are liable to degeneration as the result of syphilis—or even all of them—clinical experience yet shows that some of these groups are more prone to be affected than others, have less resistance than others. Individuals vary as to which set is affected first and to the greatest extent, but we shall not be far wrong if we place the groups in the following order, beginning with the least resistant: (1) Ciliary ganglion; (2) spinal sensory protoneurons; (3) cortical association neurons; (4) optic nerve; (5) pyramidal tracts; (6) anterior cornual cells—lower motor neurons.

If organic life could be prolonged sufficiently, independently of the

central nervous system, we might expect to find that every case of parasyphilitic nervous disease, in whatever tract it commenced, would progress more or less rapidly, to complete nervous death.

Fournier [13] apparently makes a mistake in his classification of parasyphilitic affections in including the first subdivision, for early neurasthenia after syphilitic infection is amenable to anti-syphilitic remedies, and therefore not parasyphilitic.

"But a neurasthenia occurring in a syphilitic patient in the tertiary stage is very persistent and always results in permanent disturbance of the nervous system" (Fournier). This form is never benefited by antisyphilitic remedies. Such cases are to be considered as early parasyphilis. For though as a rule parasyphilis of the nervous system does not manifest itself until eight to fifteen years after infection, yet cases of an undoubtedly parasyphilitic nature do sometimes show their first symptoms within even two or three years after infection. Parasyphilis, in fact, conforms to no rules. There is, however, I think, evidence to show the existence of a tendency, where syphilis has been acquired early in life, for parasyphilis to appear late; and where the patient is more advanced in age at the time of infection, for the interval until parasyphilis shows itself (the incubation period of parasyphilis we might call it) to be shortened. Erb [11] calls attention to this latter point; but the instances he gives are not of much value, seeing that amongst them the lowest age at which infection occurred was 48. Still in that case the "incubation period" was the longest of the series, which is as follows:—

(1) Syphilis acquired at 48, tabes developed at 58.
(2) Syphilis acquired at 57, tabes developed at 66.
(3) Syphilis acquired at 54, tabes developed at 59.
(4) Syphilis acquired at 48, tabes developed at 54.
(5) Syphilis acquired at 55, tabes developed at 57.
(6) Syphilis acquired at 55, tabes developed at 58.
(7) Syphilis acquired at 68, tabes developed at 70.

The interval of time between infection and the first appearance of symptoms of parasyphilitic nervous disease varies from three to thirty years, though exceptional cases may be found outside these limits, as in the fifth and seventh of the above series, where the interval was only two years; and in Case 9, recorded later, in which the interval was as long as fifty years. But the average is eight to fifteen years; it depends on the intensity of the virus and the efficiency of the resistance. *Ceteris paribus*, one would expect the incubation period

to be longer when the disease is acquired young, for the younger the patient the greater will be his resistance, and the longer will he be able to hold out against the enemy. On the other hand, cerebral and spinal syphilis may occur at any period after infection, and a large number suffer before they are 25 years old.

In congenital cases the first manifestation of parasyphilis usually occurs about puberty, but this is by no means constant, for it may develop much earlier, as in Still's cases quoted above [50], and it may well be that some of the cases of parasyphilis developing during the third decade, where acquired syphilis is denied and cannot be demonstrated, are due to hereditary disease. It would even seem possible that some much later cases are of the same type, for Christian Müller [36] has recorded two virgins who developed general paralysis at the end of the fourth decade and died therefrom at the ages of 42 and 43 respectively.

Fournier considers as parasyphilitic all cases of epilepsy in which the first symptom appears after the age of 35 years. Rumpf [48] puts the same proposition less dogmatically, and says that it is rare for epilepsy occurring after the age of 30 and progressing to motor paralysis to be other than parasyphilitic.

Fournier gives the following example: A man, aged 45, who had suffered from a mild attack of syphilis twenty years previously, suddenly developed *grand mal*, which recurred at intervals for many years, with frequent attacks of *petit mal* interspersed. He exhibited no other symptoms. Max Nonne [37] says he has seen several such cases, and relates two where epilepsy preceded locomotor ataxia. (1) A man, aged 45, two and a half years after infection with syphilis developed epileptic attacks occurring three or four times a month. A year later primary optic atrophy appeared and lightning pains, the case progressing to one of tabes. (2) A man, aged 40, four years after infection developed epilepsy. Three years later he developed definite tabes with absent knee-jerks, typical pupils and ataxy. Neither of these cases was affected by mercury or potassium iodide. Head [20] records a case which is probably one of parasyphilitic epilepsy. A man, aged 39, had a chancre thirteen years previously, for which he was treated with mercury for eighteen months. Three years after infection he began to have attacks of minor epilepsy consisting of momentary unconsciousness. Six years later attacks of *grand mal* began. Each attack was preceded by hours or days of intense headache. The jaw went over to the right and unconsciousness followed. There were no

abnormal signs in the nervous system; the discs were normal. Further discussion of parasyphilitic epilepsy, interesting though it is, would be outside the scope of this paper, and I will proceed to deal, *seriatim*, with the various subdivisions into which I have previously tabulated my subject. It will, however, be more convenient to take them in a different order.

Chapter III.—Tabo-paresis as the Prototype of Combined Parasyphilitic Disease of the Nervous System.

If tabes and general paralysis are simply different manifestations of one polymorphic disease—if, in fact, they are really one disease, it is perfectly simple to understand the combination of symptoms which we see in cases of tabo-paresis. Though the variations are so numerous they are governed by the varying intensity of degeneration at different points throughout the affected neuronic systems. When we consider how many different functions may be influenced more or less seriously by degeneration of the posterior columns of the cord, or of the association neurons in the cortex, we see why tabo-paresis does not conform to one type—why, indeed, it is almost impossible to find two cases precisely alike. When the two factors are subject to almost innumerable variations, the results of their union must be more variable still. And so we find general paralytics with absent ankle-jerks, or with ataxic gait, or with perforating ulcers, or lightning pains, or loss of sexual power, or exhibiting Romberg's sign, or with two or three or all of these together, indicating decay of the spinal sensory tracts in addition to cerebral degeneration.

Case 1 is an example of general paralysis of the insane with one sign of tabes.

Alfred G., aged 50, had syphilis when 18. He gives a positive Wassermann reaction as well as the cerebrospinal precipitation tests. He has well-marked mental signs and tremors of general paralysis, his pupils are unequal, irregular and of the Argyll-Robertson type. There is slight ptosis on both sides. His gait is normal but his knee-jerks are absent.

Case 2 is a similar instance in a man who gave no history of syphilis.

George C., aged 38, gives a positive Wassermann reaction both with serum and cerebrospinal fluid; the latter also shows lymphocytosis and gives the precipitation tests. He has the mental symptoms—tremors and slurred speech—of general paralysis. His pupils are unequal, irregular and of the Argyll-Robertson type. His gait is normal but his knee-jerks are absent.

The tabetic signs may be, much more rarely, manifested in the upper extremities and not in the lower. A genera' paralytic may exhibit Biernacki's sign, that is, loss of sensibility to pressure on the ulnar nerve behind the elbow; or he may be anæsthetic over the distribution of the ulnar nerve; he may have loss of joint sense, not knowing where his limbs are placed without looking; or loss of muscle sense, being unable to distinguish between the weights of different objects of similar size; or he cannot, with his eyes shut, recognize an object placed in his hand; or his arms may be inco-ordinate in their action. On the other hand, we may have a tabetic patient who has, in addition, one or more signs of general paralysis of the insane. Perhaps he has grandiose ideas, or his speech becomes slurred; or he develops tremors of the tongue or lips, or some form of aphasia may appear. Naturally tabo-paretics are as liable to have Argyll-Robertson pupils as patients suffering from general paralysis or tabes uncombined.

Case 3.—Here the spinal symptoms were the more marked.

Henry C., aged 47. He admitted syphilis but could not tell the date. Wassermann reaction is positive and his cerebrospinal fluid shows lymphocytosis and the precipitation tests. His gait is ataxic, he exhibits Romberg's sign, he has a perforating ulcer, and his knee-jerks are absent. His pupils are unequal, irregular and of the Argyll-Robertson type. He further shows distinctly the mental signs of general paralysis of the insane.

Case 4 is similar but without a history of syphilis.

Frederick P., aged 45. Wassermann reaction and cerebrospinal precipitation tests positive. His gait is unsteady, he shows Romberg's sign, and his knee-jerks are absent. His pupils are unequal, irregular and of the Argyll-Robertson type. In addition he has the mental symptoms and slurred speech of general paralysis well marked, but there are no tremors.

Such, then, is the picture when the two commonest manifestations of the one polymorphic disease are combined together.

Of the three conditions—primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy—the first is by far the most common. It is so frequently found in conjunction with tabes, and is so often manifested in congenital syphilitics, that, although some neurologists—notably Mott—recognize it as "merely a different aspect of the same polymorphic disease," it is surprising that it has not long ago been generally accorded a position amongst parasyphilitic manifestations. Yet when it has occurred in combination it has simply been considered as a symptom, and when alone frequently as "optic atrophy of unknown cause."

Chapter IV.—Primary Optic Atrophy as a Parasyphilitic Manifestation, either combined or alone.

(*a*) *Primary Optic Atrophy combined with Tabes.*

Just as we saw, in speaking of tabo-paresis, that there is the utmost variety in the cases according to the exact position and extent of the neuronic degeneration, so in primary optic atrophy with tabes we may have every gradation in the intensity of tabes shown, from mere loss of tendo-Achillis jerks to well-marked locomotor ataxia.

Norris and Oliver [38] compute that 20 per cent. of tabetics have primary optic atrophy, though Osler [40] suggests only 10 per cent. This usually develops in the pre-ataxic stage; but it may precede the first symptom of tabes by from two to twenty years, and occasionally does not occur until the late stages of that disease.

Case 5.—Here primary optic atrophy is the first manifestation and tabes is only just commencing (Turtle [52]).

A man, aged 37, had syphilis seventeen years ago. His sight began to fail four years ago, and for the last four months he had shooting pains in the left leg. There was marked primary optic atrophy, most advanced in the left eye. The pupils reacted to light. There was slight Rombergism and ataxia. The tendon reflexes were normal except that the right knee-jerk was diminished.

Case 6 is an example of primary optic atrophy with absent ankle-jerks.

William H., aged 35, contracted syphilis sixteen years ago and gives a positive Wassermann. His sight began to fail two and a half years ago, and his left eye is now quite blind. There is primary optic atrophy in both eyes, the left more advanced. There is some ptosis. His pupils are unequal, eccentric and of the Argyll-Robertson type. He is not ataxic and Romberg's sign is not present, though he cannot stand on one leg with the eyes shut. His knee-jerks are present but the ankle-jerks are lost.

Case 7.—Here the tabes is more marked. As this man has no perception of light the loss of pupil reflex to light may be ignored.

Edward T., aged 27. No history of syphilis, but there is a question whether he is not the subject of congenital disease. He gives a positive Wassermann. He gradually lost his sight nine years ago, and is now quite blind. Primary optic atrophy was the diagnosis of the oculist who saw him at the time. Six years ago he began to suffer from lightning pains. His pupils are unequal, irregular and of the Argyll-Robertson type. Romberg's sign is present, and the ankle-jerks are absent. (This man's wife has suffered from keratitis, but has had no miscarriages.)

Case 8 shows tabes still more advanced.

Edward M., aged 33; acquired syphilis fourteen years ago. Gives a positive Wassermann. Failing sight first symptom. There is primary optic atrophy in both eyes, the pupils are of the Argyll-Robertson type. He suffers from vesical crises, his gait is ataxic, Romberg's sign is present, and the ankle-jerks are lost.

Case 9.—This man is interesting on account of the extreme delay in development of parasyphilis.

George B., aged 66, had syphilis fifty years ago. He gives a positive Wassermann. Pupils unequal and fixed. Primary optic atrophy in the left eye. Paresis of the left internal rectus. Both knee- and ankle-jerks are absent. There is ulnar anæsthesia, and analgesia of the calves.

(*b*) *Primary Optic Atrophy combined with General Paralysis.*

This combination is by no means so common as the last, primary optic atrophy being present in not more than 4 per cent. of pure general paralytic patients; but it is present in a very considerable proportion of tabo-paretics, and of juvenile general paralytics. Most of the latter find their way into idiot asylums, *via* the blind schools, as epileptic imbeciles. Here again we may find one case where primary optic atrophy develops in the course of typical general paralysis, and another where the optic atrophy was the first and most definite manifestation of parasyphilis; the latter being by far the commoner.

Case 10.—Mott [35] records the following example amongst others:—

A girl, aged 15, the subject of hereditary syphilis, was bright and intelligent up to 13. She then developed double primary optic atrophy, and went quite blind. She is now mentally and physically infantile, wet and dirty. Her knee-jerks are unobtainable owing to rigidity of the legs. The pupils do not react to light. She is suffering from progressive dementia.

Case 11.—A woman mentioned by Head [21]:—

E. L., aged 23. The subject of congenital syphilis (Hutchinson teeth, scars at angles of mouth). At 6 years' of age she went blind from primary optic atrophy. At 20 she degenerated mentally; from being amenable and industrious, she became careless and incompetent. There is no paresis, the reflexes are normal, but her tongue is slightly tremulous.

(*c*) *Primary Optic Atrophy alone.*

Primary optic atrophy is a disease of fairly frequent occurrence, and although it is often found in the subjects of congenital syphilis, when it is met with in the adult it is not usually looked upon as parasyphilitic, even where there is no suspicion of diabetes or other accepted cause.

The following cases I think strongly suggest its parasyphilitic character; none of them had any symptoms of neuronic degeneration beyond the optic atrophy.

Case 12.—Sidney P., aged 28, had syphilis ten years ago. Gives a positive Wassermann. His pupils are normal, but he has double primary optic atrophy. All his tendon reflexes are normal.

Case 13.—James L., aged 49. No history of syphilis, but he gives a positive Wassermann. He has Argyll-Robertson pupils and primary optic atrophy. His deep reflexes are normal.

Case 14.—William E., aged 40. No history of syphilis, but he has given a positive Wassermann reaction three times. His cerebrospinal fluid shows no lymphocytosis. He has double primary optic atrophy. His pupils are normal, though they react only sluggishly to light. All his reflexes are normal. Indican and glycuronic acid have been found in the urine, but no sugar by any test. He is a very heavy smoker. His wife has specific ophthalmic lesions, old corneal opacities, iritic adhesions, choroidal atrophy, but they may be congenital. She has one healthy child, and has had no miscarriages.

The next two are congenital syphilitic children, with no symptoms beyond primary optic atrophy.

Case 15.—Ellen M., aged 15. Has periosteal nodes and other evidence of hereditary disease. She gives a positive Wassermann, and her cerebro-spinal fluid shows lymphocytosis. Her pupils are dilated and fixed. She has double primary optic atrophy. All her tendon reflexes are normal.

Case 16.—Frederick H., aged 7. He shows evidence of hereditary syphilis, and gives a positive Wassermann. His pupils are normal, reacting sluggishly to light. He has primary optic atrophy. All his reflexes are normal.

Either of these two may of course develop into juvenile tabes or general paralysis, but at present there is no indication of it. In none of these five cases of primary optic atrophy was there anything, remote or immediate, except syphilis, which could be considered the cause of the condition, unless the excess of tobacco in Case 14 be so regarded.

Chapter V.—Primary Lateral Sclerosis as a Parasyphilitic Manifestation, either combined or alone.

(*a*) *Primary Lateral Sclerosis combined with Tabes.*

Instances where signs of involvement of the lateral columns are noted in conjunction with tabes have been diagnosed as postero-lateral sclerosis or ataxic paraplegia. But the tendency has been to assume some syphilitic or traumatic thickening of meninges compressing the lateral columns to account for the paraplegia, and to refuse the combined disorder admission to the jealously guarded parasyphilitic portals. It

would seem, however, simpler to explain the precisely analogous degenerations of two neuronic groups, lying side by side in the spinal cord, as due to one primal toxic influence, than to find a separate cause for each.

As with other parasyphilitic amalgamations, the intensity of the components varies within wide limits. So that cases of tabes where there are no more than one or two signs of lateral sclerosis, and of primary lateral sclerosis with very early tabes, come under the same heading as those in which both diseases are well marked. The following cases illustrate varieties of this combination.

Case 17.—In this man with primary lateral sclerosis the sensory disturbance points to the development of tabes in combination.

Robert M., aged 53. Wassermann positive. He denied all venereal disease till told of the significance of this test; he then admitted "gonorrhœa" twenty-five years ago. His pupils are normal, the knee- and ankle-jerks are exaggerated, ankle-clonus is present, and both plantar reflexes are extensor. In addition he has loss of power, with loss of tactile and painful sensations in both legs; there is difficulty in micturition, and weakness of abdominal muscles. Antisyphilitic treatment for a year was not beneficial, and injection of salvarsan gave no result.

Case 18.—Francis M., aged 29. Had syphilis six years ago, and was treated for two years. His cerebrospinal fluid shows lymphocytosis. His first symptom was staggering gait twelve months ago. A few days before admission he was thrown from a van and fell on his back. He was unable to walk for two days, but that passed off. On admission he had pain in the back (D. 12), weakness in the legs, and difficulty in starting micturition. His pupils were unequal but reacted. There was no anæsthesia. His gait was inco-ordinate and spastic. Romberg's sign was present. His knee-jerks were exaggerated, ankle clonus was present, and Babinski's sign was marked. There were no intention tremors nor nystagmus. Antisyphilitic remedies had no effect on his condition, although the pain in the back, which was probably due to the fall, disappeared.

Case 19.—William J., aged 48, had syphilis fourteen years ago. Wassermann positive, and lymphocytosis present in the cerebrospinal fluid. Four years after infection the patient was exposed to considerable hardship in the Boer War, and his right leg became weak and "dragged." This remained much the same for three years; then he had a course of antisyphilitic treatment without improvement. Six years later he gave a negative Wassermann, and was treated with Faradic baths. Twelve months after that the Wassermann reaction was positive, and he came into hospital for salvarsan treatment. The pupils are normal. Knee-jerks are absent. Plantar reflexes extensor. His gait is inco-ordinate, Romberg's sign is present, both legs are analgesic but not anæsthetic; the right leg is rather wasted, but there are no trophic lesions. He

has lightning pains. No ulnar anæsthesia. A fortnight after salvarsan injection the Wassermann reaction was negative, although it had been positive a month before. The importance to be attached to this, since the interval is so short, is doubtful.

(b) Primary Lateral Sclerosis combined with General Paralysis.

Cases have been recorded where general paralysis has developed in a patient already suffering from primary lateral sclerosis (Osler [41]), and certainly general paralytics may, and often do, exhibit exaggerated reflexes, whilst sometimes Babinski's sign is well marked.

Case 20.—Frank L., aged 28, had syphilis six years ago; he gives a Wassermann reaction with both serum and cerebrospinal fluid. The latter shows lymphocytosis and gives the precipitation tests. He has the mental symptoms and tremors of general paralysis. His pupils are irregular, but react. His gait is normal; his knee-jerks are present; there is no ankle clonus, but the plantar reflexes are extensor.

Case 21.—Thomas B., aged 39. He gives no history of syphilis, but the Wassermann reaction is positive, and the cerebrospinal fluid responds to the precipitation tests. He has the mental symptoms, slurred speech and tremors of general paralysis. There is marked intention tremor in the right arm. The elbow-jerks are absent; the pupils are unequal and irregular, but react. There is slight ptosis. His gait is unsteady and inco-ordinate; his knee-jerks are exaggerated, ankle clonus is present, and the plantar response is extensor.

Case 22.—Here is a case, recorded by Poynton [44], in which general paralysis and primary lateral sclerosis are combined in a child, the subject of congenital disease.

A girl, aged 11, with Hutchinson's teeth and patches of choroiditis. She has degenerated mentally, morally, and physically for two years, becoming dirty and silly. Her tongue is tremulous. Her pupils are unequal and fixed. She is unable to walk on account of spastic paraplegia, which is more marked in the left leg than the right. The upper extremities are normal, but the deep reflexes in the legs are increased, and Babinski's sign is present in the left foot.

(c) Primary Lateral Sclerosis combined with Primary Optic Atrophy.

This will at first sight be diagnosed as disseminated sclerosis. But instances occur in which there is primary optic atrophy with spastic paraplegia or Babinski's sign, and no other sign of dissemination, in patients past the usual age for disseminated sclerosis. These may well be really a combination of two of the rarer forms of parasyphilis

and not a haphazard insular degeneration at all. Both the cases below, in illustration of this amalgamation, came under observation before Wassermann's reaction had assumed importance.

Case 23.—Henry C., aged 69, had syphilis forty years previously. His pupils were normal, there was ptosis and ophthalmoplegia of the external rectus, both on the right side. His vision was blurred and he proved to have double primary optic atrophy. Romberg's sign was present, his left knee-jerk was exaggerated, the right one diminished, and Babinski's sign was present.

Case 24.—Agnes N., aged 41, a married woman, giving a history of "vaginal trouble" some years previously. She had double primary optic atrophy. The pupils were normal, there was no nystagmus. The knee-jerks were exaggerated, ankle clonus was present, and the plantar reflexes were extensor.

(d) Primary Lateral Sclerosis alone.

Some cases of primary lateral sclerosis give a history of syphilis, but no reliance can be placed on statistics in this condition unless Wassermann's test has been applied or a *post-mortem* examination made, for so many cases diagnosed as primary lateral sclerosis are found *post-mortem* to be secondary to cerebral tumour or other unsuspected cause. It is probable that nearly every, if not every, instance of uncomplicated primary sclerosis of both lateral columns is parasyphilitic; but such examples are not common.

Case 25.—Alfred D., aged 64, had syphilis forty years ago and gives a positive Wassermann. Disease began a year ago with weakness of the legs. Six weeks ago paralysis of the right external rectus showed itself. His pupils are normal. His gait is spastic: Achillis jerks brisk; Babinski's sign is present.

Case 26.—Here is a case of early primary lateral sclerosis with Argyll-Robertson pupils.

James T., aged 43, had syphilis twenty-five years ago and now gives a positive Wassermann. His pupils are unequal, irregular, eccentric and of the Argyll-Robertson type. There is slight ptosis. The ankle-jerks are exaggerated with a tendency to clonus. The plantar response is flexor in the right foot and unobtainable in the left. He cannot stand on one leg with the eyes shut. There is spasticity of the ankle-joints with a tendency to stand always on tiptoe.

Case 27.—Winifred E., aged 29, a married woman who has had one miscarriage and gives a positive Wassermann reaction. The elbow-, knee- and and ankle-jerks are all exaggerated and Babinski's sign is present. Her eyes are normal, and there is no nystagmus nor any other sign of insular sclerosis.

Case 28.—Edward C., aged 38. No history of syphilis but gives a positive Wassermann. His pupils are normal. The legs are spastic, knee-jerks exaggerated, ankle clonus present, plantar reflexes extensor.

Case 29.—James H., aged 54, had syphilis twenty-five years ago. Wassermann reaction positive. Pupils are normal. There is slight tremor of the tongue. Romberg's sign is present. His knee-jerks are increased, ankle clonus is present and the plantar reflexes are extensor.

Case 30.—Here is an interesting case, recorded by Grainger Stewart [49] as "chronic syphilitic meningitis with compression of the cord," which I think is more probably an example of parasyphilis of the variety under consideration, for the pupils do not react to light, though they do to accommodation. There is also some sensory disturbance which may be the first sign of the supervention of tabes.

A man, aged 64, had syphilis forty-six years ago. Ten years ago he fell unconscious in the street, the unconsciousness lasting fifteen minutes. There was no paralysis or other after-effect from this incident, and it is doubtful whether it has any connection with the ultimate condition. Five years later his legs became stiff and he developed into an example of spastic paraplegia. The knee- and ankle-jerks are exaggerated, ankle clonus is present and the plantar response is extensor. The pupils are of the Argyll-Robertson type. Motor weakness is slight. The abdominal and epigastric reflexes are absent, and there is slight diminution of all forms of sensibility below the fourth dorsal segment. Nothing abnormal is found in the spine.

Chapter VI.—Progressive Muscular Atrophy as a Parasyphilitic Manifestation, either combined or alone.

(*a*) *Progressive Muscular Atrophy combined with Tabes.*

Quite early in this paper I referred to Dejerine's [8] estimate that 20 per cent. of tabetics exhibit some form of muscular atrophy, and to the fact that progressive muscular atrophy is becoming more and more frequently recognized in France as a parasyphilitic manifestation. Still as a rule the muscular atrophy is looked upon as one of the less frequent symptoms of tabes, or else it is saddled on to one or other of the etiological pack-horses, usually "hard work." Kinnier Wilson [53], however, in recording the following case, says that he considers "tabetic muscular atrophy is neither a symptom nor a complication of tabes, but an associated condition of syphilitic origin."

Case 31.—A man, aged 37, had syphilis twenty-two years previously. He had been troubled with lightning pains for ten years, girdle pains for nine

years and wasting of the small muscles of the hands (starting in the right) for seven years. He had gastric crises, and experienced abnormal fatigue in the legs. His pupils were of the Argyll-Robertson type, the deep reflexes absent. There was extreme wasting of the thenar and hypothenar muscles, with no reaction to faradism or galvanism. The interossei were less wasted; there was no great wasting in the arms, though they were weak. In the legs all the muscles, particularly the anterior tibial groups, were small and weak. Sensation of pain was impaired in the ulnar distributions, and almost lost in the legs. There was loss of tactile sensibility over the trunk and legs. His right ankle was an incipient Charcot joint. The pathological report of this case records that there is great reduction in the cells of the anterior horns, the change being atrophic or sclerotic. What cells remain are mostly shrunken. The side where the muscular atrophy was most obvious (i.e., the right) shows the greater changes in the cord.

Case 32.—This is an instance of early progressive muscular atrophy in a tabetic patient.

George S., aged 44, gives no history of syphilis, but the Wassermann reaction is positive. His pupils are irregular and of the Argyll-Robertson type. His Achillis-jerks are absent. He has perforating ulcers, rectal crises and anæsthesia of the bladder (he does not know when it is full). The tongue is tremulous, and there is marked weakness and wasting of the intrinsic thumb-muscles of both hands.

Case 33.—Here is a case where the lower neuron degeneration is affecting the bulbar nuclei.

Charles H., aged 36. No history of syphilis, but he gives a positive Wassermann. He has Argyll-Robertson pupils. The ankle-jerks are absent and Romberg's sign is manifest. He has difficulty in swallowing owing to paralysis of the muscles of the soft palate. (No history of diphtheria could be elicited; the patient denied having a sore throat.)

(b) Progressive Muscular Atrophy combined with General Paralysis.

I have met with well-marked cases of this combination. As a rule, when muscular atrophy occurs in general paralysis of the insane it is considered as an unusually marked example of the weakness which comes on in the ordinary course of that disease.

Case 34.—Henry P., aged 34, had syphilis eighteen years ago, and gives a positive Wassermann and the cerebrospinal precipitation tests. He shows the mental symptoms, tremors and slurred speech of general paralysis. There is slight ptosis, and the pupils are unequal, irregular and of the Argyll-Robertson type. His gait is unsteady, and his knee-jerks are absent. There is extreme wasting of all muscles (most marked in the interossei) of the right

hand and of the same shoulder. All the muscles, except the interossei and lumbricales of the right hand, react to faradism and galvanism, though both are diminished, especially in the right arm and shoulder, and particularly in the right infraspinatus. The interossei of the left hand are also affected.

Case 35.—James Q., aged 50, admits syphilis, but does not know the date. Wassermann reaction positive, cerebrospinal fluid gives precipitation tests, and shows lymphocytosis. There are tremors of the tongue and lips. He is very grandiose and happy. He has slight right-sided ptosis; his pupils are unequal, irregular and fixed. His knee-jerks and all other deep reflexes are lost, as also are the cremasteric and abdominal. The interossei of both hands are wasted, and there is some motor impairment of the right arm.

(*c*) I have not encountered a satisfactory instance of the combination of progressive muscular atrophy with primary optic atrophy.

(*d*) *Progressive Muscular Atrophy combined with Primary Lateral Sclerosis.*

Here we have the condition known as amyotrophic lateral sclerosis; or, when the degeneration extends to, or occurs at, the upper end of the cord and medulla, progressive bulbar paralysis. If the symptom-complex comprising progressive muscular atrophy, amyotrophic lateral sclerosis and progressive bulbar paralysis be considered as one primary degeneration of the motor neurons, both upper and lower, we see how cases may vary according to what point in the group is first attacked, and to what extent the disease spreads thence throughout the group. It may begin in the anterior cornual cells and confine itself to that system, giving simple progressive muscular atrophy; or it may extend to the pyramidal tracts, giving amyotrophic lateral sclerosis; and later the bulbar nuclei and the hypoglossal nerve may be involved, thus adding bulbar paralysis, which, fortunately for the victim, as a rule rapidly carries him off. But the trouble sometimes starts with bulbar paralysis, and may show evidence, before the patient dies, of downward spread.

In 1850, Aran [1] first described progressive muscular atrophy starting in the intrinsic muscles of the hands. In 1859, Duménil [9] noted progressive bulbar paralysis with atrophy of the hypoglossal nerve, and regarded it as a form of progressive muscular atrophy. In 1872, Charcot [6] described amyotrophic lateral sclerosis, considering it also as an extension of progressive muscular atrophy.

With regard to the etiology of these varieties of motor-tract degeneration, Dana [7] and Merle [27] urge syphilis as the essential

cause, whilst Wilson [54] (in 1907) considers lead poisoning the commonest factor, and thinks that in some cases syphilis can be excluded. Gowers [17] thinks there is some evidence of heredity. The points in favour of parasyphilis are the age-incidence (in the parasyphilitic decade—the fourth), the greater frequency with which men are attacked than women, and the fact that Argyll-Robertson pupils are sometimes associated.

Case 36.—William V., aged 52, does not admit syphilis, but gives a positive Wassermann reaction. He gives a four years' history of general progressive weakness and loss of control of the legs: "Feet catch in everything." He complained that his feet and legs were numb, and of cramps in the feet, legs, thighs and hands. There is no absolute paralysis, but general paresis. His tongue is not tremulous, but his speech is altered and his voice falsetto. The pupils are normal and react, if anything, better to light than to accommodation. Sensation is unimpaired. His knee-jerks are present: the left ankle-jerk is increased, the right absent. The plantar reflex is extensor in the left foot, unobtained in the right. The cremasteric and abdominal reflexes are present. There is well-marked wasting of both thenar eminences, and he cannot oppose the thumb and little finger. There is some wasting noticeable in the left leg.

Case 37.—William B., aged 50; he had syphilis thirty years ago, and has been troubled for nineteen months with weakness of the left hand, for six months with the same in the right hand, and lately with weakness of the left leg. In the left hand there is marked wasting and loss of power in all the intrinsic muscles; also in the forearm, both flexors and extensors; there is very little movement in the elbow-joint, and practically none in the shoulder. The atrophy in the right hand is much less marked. Reaction of degeneration is present in all the affected muscles, and is complete in the interossei of the left hand. The legs are weak, but show no obvious wasting. His knee-jerks are exaggerated; both ankle-clonus and Babinski's sign are present.

(*e*) *Progressive Muscular Atrophy alone.*

As a parasyphilitic manifestation progressive muscular atrophy is certainly most often met with in combination; but the fact that the knee-jerks may be lost in this condition quite early has probably led to a considerable proportion of these cases being diagnosed as locomotor ataxia with marked muscular symptoms.

Case 38 shows this liability, as the tendon reflexes are absent, although the muscular atrophy is confined, clinically, to the upper extremities. Probably some change is present in the cord lower down, some shrinkage of anterior cornual cells.

Thomas F., aged 53, had syphilis thirty-five years ago. Wassermann reaction positive. His pupils are irregular but react, though very faintly only,

to light. The deep reflexes are lost. There is no ataxy. Wasting is evident in both upper limbs in the interossei, thenar, and hypothenar eminences, the flexors and extensors of the forearms, the muscles of the upper arms and shoulders. The legs are unaffected.

Case 39.—Joseph A., aged 50, had syphilis thirty years ago. His pupils are unequal but react. The right knee-jerk is absent, the left present. The thenar and hypothenar eminences are wasted, especially of the right hand, also the interossei, the flexors of arms and upper arms, the supra- and infra-spinati and the lower part of the pectoralis major. The right thigh is also much wasted.

W. Harris [18], treating of syphilis of the spinal cord, mentions cases of chronic or subacute poliomyelitis due to syphilis. These he says are "generally mistaken for progressive muscular atrophy." He refers to three cases, recorded by Max Nonne, in which the upper extremities only were affected; and three by J. Hoffmann. But Hoffmann [22], at all events, is one of those who recognize progressive muscular atrophy as a parasyphilitic manifestation. Harris also describes the following case of his own :—

Case 40.—A woman (age not given), with a definitely positive Wassermann, had pain in the left upper arm as the first symptom of disease, followed by paralysis of the deltoid. A year later her right wrist dropped, and the right shoulder became paralyzed. A year later there was almost complete paralysis of both deltoids, biceps, spinati, and extensors of the forearm, with reaction of degeneration. There was no sensory disturbance; all the deep reflexes except the jaw-jerk were absent, and the pupils reacted sluggishly to light.

The Wassermann reaction and the slowly progressive nature of the complaint suggest a diagnosis of parasyphilitic progressive muscular atrophy. I fail to see on what grounds a special class need be devised for "Cases generally mistaken for progressive muscular atrophy."

Rose et Rendu [46], in the interesting article already referred to, describe two cases in which no cause but syphilis could be suggested. In the first they hold that, in spite of some exaggeration of reflexes and a tendency to ankle clonus, it is a case of pure progressive muscular atrophy. But these signs should rather be held to point to some involvement of the pyramidal tracts, and as suggesting the development of the case into amyotrophic lateral sclerosis.

Case 41.—A man, aged 42, except for syphilis at 18, never had any illness. He was treated for two years, and married at 26. His wife's first pregnancy resulted in miscarriage. Some difficulty in using his hands appeared six years

ago. This paresis progressed, and two years later spread to the arms successively. He has no pain, but some alteration of sensibility to cold. No urinary trouble, but loss of sexual power for the last year. The thenar and hypothenar muscles of both hands are very markedly atrophied, also the first interossei. Atrophy not so marked in the forearms, affecting the extensors and supinators only in the right, but the flexors, too, in the left. The elbow-jerks are exaggerated. The legs are unaffected, except that the reflexes are somewhat exaggerated, with a tendency to ankle clonus on both sides. Plantar response flexor. The right cremasteric reflex is absent. The pupils are of the Argyll-Robertson type; and there is an intense cerebrospinal lymphocytosis.

The second case differs from the above in that all the deep reflexes are absent, and is a pure example of progressive muscular atrophy alone.

Case 42.—A man, aged 34, had syphilis at 21. Three years later he had lightning pains. Six years after infection the right hand began to get weak and waste, the thumb being first affected. Four years later the left hand followed suit and the forearms and arms became involved. There was progressive loss of power before the atrophy appeared. The trophic changes are confined to the upper limbs, being most marked in the thumb-muscles of the right hand, and the interossei of the left. The right arm is almost useless, the left not so advanced. The deep reflexes are absent in all four limbs, the superficial ones remaining. There are no abnormalities of sensation; no ataxia; Romberg's sign is not present, and there are no sphincter troubles. The pupils are unequal, and are described as "incomplete Argyll-Robertson." There is no optic atrophy. The cerebrospinal fluid shows lymphocytosis. No benefit has accrued from anti-syphilitic treatment.

Chapter VII.—Cases where Manifestations of Degeneration in more than Two Nerve Tracts occurred in one Individual.

In studying these parasyphilitic nervous diseases one is constantly aware of a suspicion that more tracts are involved than is manifested at first sight. Some abnormality of sensation, some failure of vision, some change in moral or intellectual characteristics, some lately developed jerkiness of movement, some loss of power in the hands, or an alteration in the voice, may attract the attention and suggest that the decay is not confined to one or even two communities of neurons.

For this reason it is often very difficult to classify a case; and having classified it, one is frequently tempted to remove it to some other group. Parasyphilis of the nervous system must be considered, in fact, as one polymorphic disease with many different manifestations. The clinical picture is almost kaleidoscopic in its infinite variety. Taking only the five manifestations dealt with in this paper, the diagrammatic repre-

sentation of their combinations in pairs is well-nigh confusing, and would be entirely so were the multiple conditions now to be considered indicated.

Yet, in a full consideration of parasyphilis of the nervous system, room must probably be found for certain neurasthenias, dystrophies, non-developments and epilepsies, with their associations.

Of multiple manifestations one would naturally expect the greater number to be based on tabo-paresis; and such is the case. I shall not describe more than one instance of each variety.

Case 43.—Tabo-paresis with primary optic atrophy.

John S., aged 50, denies syphilis but has a scar on the glans penis. He gives a positive Wassermann both with blood and cerebrospinal fluid; the latter further shows lymphocytosis and gives the precipitation tests. He has the mental symptoms of general paralysis, with slurred speech and tremors of the tongue, lips and hands. His gait is unsteady, and his knee-jerks are absent. His Argyll-Robertson pupils are irregular in outline, and there is primary optic atrophy in both eyes, especially in the left.

Case 44.—Tabo-paresis with primary lateral sclerosis.

George C., aged 33. He had syphilis thirteen years ago and gives a positive Wassermann reaction. He now shows the mental symptoms of general paralysis: his speech is defective, his tongue tremulous, his pupils irregular and of the Argyll-Robertson type. He does not exhibit Romberg's sign, but both his knee- and ankle- jerks are absent. Finally the plantar reflex is extensor in both feet.

Case 45.—Tabo-paresis with progressive muscular atrophy.

George E., aged 45. No history of syphilis was obtained, but he gave a positive Wassermann, and his cerebrospinal fluid gave the precipitation tests. He has the mental signs of general paralysis of the insane with tremulous tongue and lips, and slurred speech. In addition there is ptosis on the left side; his pupils are unequal, irregular and of the Argyll-Robertson type. His gait is ataxic, and his knee-jerks are absent. There is marked progressive trophic wasting of the right thigh and calf-muscles.

Case 46.—General paralysis of the insane with amyotrophic lateral sclerosis.

Sophie P., aged 43. No history of syphilis, but her cerebrospinal fluid gave both the precipitation tests and the Wassermann reaction. She has the mental signs, tremors, and defective speech of general paralysis. Her pupils react to light and accommodation, though very slightly to the former. Her legs are inco-ordinate. The knee-jerks are present, and there is ankle clonus

and extensor plantar reflex on the left side. There is great progressive muscular wasting of both arms and legs.

Case 47.—Tabo-paresis with primary optic atrophy and primary lateral sclerosis. Here four nerve-tracts show evidence of decay. This man had a very severe attack of syphilis, with troublesome sores all over the body.

John W., aged 46, had syphilis twenty years ago; his wife has had numerous miscarriages. He gives a double Wassermann reaction and his cerebrospinal fluid also exhibits lymphocytosis and the precipitation tests. He is demented, his tongue and fingers are tremulous. He is inco-ordinate, though his gait is fair. The tendon reflexes in both legs and arms are absent. Babinski's sign is present. He has double primary optic atrophy, and his pupils are unequal, irregular and of the Argyll-Robertson type.

Tooth and Howell [51] publish an exhaustive account of a very severe case of amyotrophic tabes from the point of view that the tabes and muscular atrophy are due to two distinct causes, though the separate and distinct cause of the latter is not clearly indicated. I bring my series of cases to an end with an abstract of this one because it appears evident to my mind that it is an instance of parasyphilis of the nervous system exhibiting signs of degeneration in four separate nerve-tracts. One of these, however, the pyramidal, was not indicated during life, or was overshadowed by the intensity of the other troubles.

Case 48.—Tabes with primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy.

A man, aged 35, had syphilis sixteen years before. For sixteen months there has been progressive difficulty in walking and numbness of the feet. He is mentally bright, but physically troubled with lightning pains, girdle pain, gastric crises, difficult micturition, right-sided ptosis, and failing vision, especially in the left eye. Articulation lisping. Tongue tremulous, left half atrophied. Unequal Argyll-Robertson pupils. Discs distinctly suggestive of primary optic atrophy. Almost complete ophthalmoplegia of both eyes. Some paresis of lips. Hearing defective in both ears. Left masseter muscle wasted. Muscular power in arms and trunk fair, legs very weak and atrophied, the right more so than the left. Can only just stand with support, and attempts to walk only result in disordered ataxic movements. Muscle-pain sense lost, joint-sense defective. Analgesia over greater part of face and body, most marked in ulnar distribution and outer sides of legs. Marked inco-ordination in the arms as well as legs. All the above symptoms were progressive, and the right side of tongue, the right masseter muscle, and both temporal muscles became involved in the atrophy, and deglutition became increasingly difficult.

Pathological examination showed that the third, fifth, sixth, and twelfth cranial nerves were wasted. The pia arachnoid was a little thicker over the posterior columns in the cervical and upper dorsal region. Both posterior and anterior nerve-roots were small. The anterior cornual cells were diminished in number, and those remaining were shrunken. The degeneration of posterior columns was typical of tabes, and there were slight degenerative changes in the lateral columns. The affected muscles showed changes identical with those of progressive muscular atrophy, though the eye-muscles were very little altered.

Summary.

There is no doubt that in the vast majority of cases of tabes and general paralysis of the insane syphilis is the essential cause. They are parasyphilitic nervous diseases.

There is evidence that at all events some cases of primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy, are parasyphilitic too. A history of syphilis or a positive Wassermann reaction, and in some instances the *post-mortem* examination, point to this being so.

In tabes and general paralysis there is degeneration of certain neuronic tracts or groups; and degeneration of precisely the same character in other neuronic groups produces primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy.

Combinations of all three with tabes or general paralysis of the insane, or with both, or amongst themselves, are so frequent that it is difficult to withstand the conclusion that their essential etiological factor is the same, more especially since it is conceded that syphilis has a great affinity for the nervous system.

If it be allowed that the neuronic degeneration of primary optic atrophy, primary lateral sclerosis or progressive muscular atrophy when combined with that of tabes or general paralysis is due to syphilis, it cannot be denied that such degeneration, occurring uncombined, may still be parasyphilitic.

The Argyll-Robertson pupil is recognized as a symptom of tabes and general paralysis, in other words it is a parasyphilitic manifestation. It is found also with primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy.

If the question of antecedent syphilis were carefully investigated in every case of primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy, or better still if every case were subjected

to Wassermann's test as well, I believe that an accumulation of evidence, entirely analogous to that obtained in determining the etiology of tabes and general paralysis, would soon be at hand, and that these three diseases, at present wandering in the Wilderness of Undiscovered Causes, would take their rightful place amongst the rarer manifestations of parasyphilis of the nervous system.

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[47] RUMPF. *Berl. klin. Wochenschr.*, 1881, Bd. xviii, S. 521.
[48] *Idem.* Quoted by Mott. *Op. cit.*, p. 197.
[49] STEWART, GRAINGER. *Proc. Roy. Soc. Med.*, 1909-10, vol. iii (Neurol. Sect.), p. 33.
[50] STILL. "Common Disorders of Childhood," London, 1909, p. 516.
[51] TOOTH and HOWELL. *Proc. Roy. Soc. Med.*, 1911-12, vol. v (Neurol. Sect.), p. 81.
[52] TURTLE. *Proc. Roy. Soc. Med.*, 1908-9, vol. ii (Neurol. Sect.), p. 104.
[53] WILSON, S. A. KINNIER. *Proc. Roy. Soc. Med.*, 1908-9, vol. ii (Neurol. Sect.), p. 20.
[54] *Idem.* *Rev. of Neurol. and Psychiat.*, 1907, vol. v, p. 441.

Publications Recently Received.

[Notes on a book under this heading do not preclude a subsequent review.]

The Pituitary Body and its Disorders. By Harvey Cushing, M.D., Professor of Surgery, Harvard University. Pp. 341, with 319 illustrations. Philadelphia and London: Lippincotte, 1912.

This remarkable work is the fruit of a series of researches carried out by Professor Harvey Cushing in conjunction with his colleagues and assistants in the Johns Hopkins Hospital. A short account is first given of the anatomy and physiology of the pituitary body, of which the posterior portion pours its secretion into the cerebrospinal fluid, whilst the anterior part acts with the other ductless glands. Then cases of disease are analyzed and shown to be due to excess, to diminution, or to defective pituitary activity; those patients in whom the secretion has been in excess grow to a huge size and undergo premature sexual development, while diminished activity leads to small size, adiposity, and sexual infantilism. Many cases, however, especially those due to neoplasms of the hypophysis, show first a period of excessive, followed by one of defective, activity of the glands: into this group fall some instances of acromegaly.

But the pituitary body is one of the ductless glands, and its disturbed activity may be associated with those of other similar organs. Hence arises the so-called "polyglandular syndrome," indicating that it is difficult to tell which of the glands is primarily at fault; the patient may show signs pointing to thyroid, adrenal and pituitary insufficiency.

The pathology, nature, and clinical character of tumours within the sella turcica are considered, and the various surgical and therapeutic measures for their relief are dealt with fully.

The book is one so full of interest, and the author's conclusions are so illuminating, that we cannot do justice to it in a short notice.

Die Wassermann'sche Reaktion mit besonderer Berücksichtigung ihrer klinischen Verwertbarkeit. Von Dr. Harald Boas. S. 186. Berlin: Karger, 1911.

Although not directed primarily to the problems of nervous disease, every neurologist interested in the Wassermann reaction should read this work. After a clear and concise account of the reaction and its modifications, its value is established by a large series of examinations in control cases. Then Dr. Boas deals with the reaction in primary, in secondary, in tertiary and in latent

syphilis. A chapter is devoted to each of the following conditions: tabes dorsalis, dementia paralytica and congenital syphilis. He deals with the influence of treatment on the reaction and with its practical significance from the therapeutic aspect.

Surgery of the Brain and Spinal Cord based on Personal Experience. By Prof. FEDOR KRAUSE, M.D., English adaptation by Dr. MAX THOREK. Vol. ii, with 94 figures in the text; vol. iii, with 42 figures in the text. The pages, numbered consecutively from the beginning of vol. i, reach 1197. London: H. K. Lewis. No date.

The first volume of this translation of Professor Krause's admirable work appeared in 1910 and was noticed in BRAIN, vol. xxxiii, page 267. The book is a personal record of one man's work; each condition of the central nervous system likely to come to operation is passed in review and one or more instances from the author's experience are fully described and illustrated. Thus, the present volumes deal with epileptiform attacks, Jacksonian epilepsy and the results of excision of the cortex. New growths of the brain, in all important situations, are considered on the basis of 109 cases which came to operation; the description of signs and symptoms is usually rather short and rigidly directed towards a diagnosis. The third volume is mainly occupied with an interesting series of tumours of the spinal cord, and other conditions which may simulate a new growth such as meningitis serosa acuta circumscripta.

Throughout, the illustrations, and especially the coloured plates, are excellent, in fact they form a valuable atlas of the pathology during life of the central nervous system. The English of the translation leaves much to be desired.

Die akute Poliomyelitis bzw. Heine-Medin'sche Krankheit. Von Dr. IVOR WICKMAN. S. 108. Mit 12 Textabbildungen und 2 Tafeln. Berlin: Springer, 1911.

This pamphlet, giving in short compass an account of acute poliomyelitis, is a separate publication of Dr. Wickman's article in Lewandowsky's "Handbuch der Neurologie." It forms a most useful compendium of our present knowledge and of recent researches on this disease for those who are particularly interested in poliomyelitis.

Arbeiten aus dem Pathologischen Institut der Universität Helsingfors (Finland). Herausgegeben von Prof. Dr. E. A. HOMÉN. Band iii, Hefte 2-4, S. von 91 bis 607; mit 30 Tafeln. Berlin: Karger, 1911.

This volume of researches is occupied with experiments on tuberculosis of the peripheral nerves, by Professor Homén; of the liver, by Dr. Wallgren, and by a monograph on experimental tuberculosis of the meninges and brain, by Dr. Fieandt. The plates are excellent.

Ergebnisse der Neurologie und Psychiatrie. Redigiert von Prof. Dr. H. Vogt und Doz. Dr. R. Bing. Erster Band, erster und zweiter Hefte, S. 452; mit 38 Abbildungen. Jena: Fischer, 1911.

This interesting volume starts with an account by Dr. Isserlin of the progress in psychotherapy during the last few years; a clear and remarkably fair summary is given of the treatment adopted by the various schools, with, in each case, a short statement of the views upon which it is based. This is followed by a review of the pathogenesis and symptomatology of cerebellar diseases by Professor Mingazzini. Dr. Spielmeyer deals with dementia paralytica, tabes dorsalis and sleeping sickness from the standpoint of etiology and pathology, and Dr. Kleist gives an interesting account of the present views on apraxia. We hope that these excellent short monographs will be continued, as they supply a want amongst neurologists who are not directly working at the particular subject with which they deal.

The Psychology of Insanity. By Bernard Hart, M.D. Pp. 176. Cambridge: University Press, 1912.

It is difficult to speak too highly of this little book, which forms one of the Cambridge manuals of science and literature. The author has succeeded in displaying the psychological conception of abnormal mental states so simply and clearly that it can be grasped by anyone; and yet he has avoided the crudities which overload the work of most of the psycho-analytical school. Dissociation, the nature of complexes, conflict, repression and projection are all explained, and instances are given from normal and abnormal mental states. This is one of the best of an admirable series and can be recommended to all who are interested in the problems presented by insanity.

Hypnosis and Suggestion. By W. Hilger, M.D. Translated by R. W. Felkin, M.D. With an Introduction by Dr. Van Renterghem (Amsterdam). London: Rebman. No date.

Like most works on this subject, Dr. Hilger's book begins with a somewhat elaborate introduction on the history and nature of hypnosis. This is followed by chapters on suggestion and will, the effect of suggestion on sensation and on disturbances of reflex activity. Many cures are cited, but the clinical instances are poorly related, and the trail of the example taken from "Common Knowledge" is over the book.

The Feeble-minded. By E. B. Sherlock, M.D., D.P.H. With an Introduction by Sir H. B. Donkin, M.D. Pp. 327. London: Macmillan, 1911.

The author begins with two chapters devoted to the nature and basis of mind. He then passes to the feeble mind and the anatomical abnormalities

of the brain with which it is associated. The causes and varieties of feeble-mindedness are then described, and in a final chapter he considers the methods of dealing with the feeble-minded.

Neurasthenia. By GILBERT BALLET. Translated from the Third French Edition by P. CAMPBELL SMITH, M.D. Third Edition, illustrated with 7 figures. London: Kimpton, 1911.

This is a good translation of Professor Ballet's work on neurasthenia, and gives a full description of this disease from the point of view of a French clinician. The leading symptoms are described in detail, but sometimes, as in the case of traumatic neurasthenia, the description is scarcely adequate in length. Psychasthenia is wisely eliminated, and the author insists on the necessity for exact diagnosis. The second half of the book is devoted to methods of treatment.

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To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.